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ON SPLENIC ANÆMIA.[1]

[SECOND PAPER.]

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THE question of the existence of a separate malady—anæmia splenica—is still in what may be called the tentative or inquisitive stage. The proposition which I offer for discussion is that a special malady does exist, of unknown etiology, characterized by a chronic course, enlargement of the spleen, anæmia of a secondary type, a marked tendency to hemorrhage from the stomach, and a liability in the late stages to be associated with jaundice, cirrhosis of the liver, and ascites. The conditions described as primitive splenomegaly and Banti's disease are initial and terminal stages, respectively, of this malady. The history of the question I need not discuss, as it is very fully given in the papers of Sippy[2] and of Wentworth;[3] nor it is necessary to discuss the possible connection of the malady with Hodgkin's disease or pseudo-leukæmia, with which a majority of observers rightly consider it has nothing whatever to do. In January, 1900, I reported a series of cases.[4] In the present paper I shall give (1) a few additional cases and the subsequent history of several of those previously reported; (2) an analysis of a series of cases of anæmia with enlarged spleen, furnished by members of the Association; and (3) a summary of the clinical features of the disease.

[1] Read at the meeting of the Association of American Physicians, May, 1902.
[2] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, November, 1899.
[3] Boston Medical and Surgical Journal, 1901.
[4] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1900, vol. cxix.

I.

The subsequent history of some of the cases in my previous paper may first be given:

Case X.—A man, aged thirty-nine years, was first seen June 15, 1898, with moderate enlargement of the spleen, moderate corpuscular anæmia, low hæmoglobin, and marked pigmentation. He did not know exactly how long he had had the anæmia or the enlarged spleen. I heard from him March 27, 1902. He had been in fairly good health, except that in March, 1901, he had three hemorrhages from the stomach, which, he says, nearly killed him. He was unconscious and in a state of torpor for two weeks. Following this he had ascites, and had to be tapped. At the date of writing he said he had recovered sufficiently to be able to do his work.

Case XIV.—A man, aged thirty-five years; a very typical instance, with a greatly enlarged spleen, characteristic blood condition, slight pigmentation of the skin, attacks of hæmaturia, with slight jaundice. He was last seen on April 16, 1900. The spleen was enlarged; he had been jaundiced for two weeks; edge of liver could be felt 6 cm. from the ensiform cartilage; the right lobe only felt on deep inspiration. He has been under Dr. Thayer's care, who reports this spring that he is still anæmic, but able to be at work.

Case XIII.—Mrs. C. was of exceptional interest, as there was a doubt as to whether the case was not one of pernicious anæmia, with greatly enlarged spleen. She did well in the hospital; the spleen reduced in size in a remarkable way. She left the hospital November 20, 1899. She remained well during 1900. The spleen was not below the costal border. She was readmitted in April, 1901, in a condition of the most profound and progressive anæmia, in which she died on the 26th. The blood had all the features of a pernicious anæmia. The spleen weighed only 400 grammes, and the pulp was soft and flabby. There was fatty degeneration of the heart. The liver weighed 1500 grammes. The bone-marrow was of a deep gray-red color. The blood condition on her first admission (see first paper), the remarkable improvement with rest and arsenic, the complete disappearance of the symptoms, and the enlargement of the spleen, the relapse, with profound and fatal anæmia, leave no doubt, I think, that this belongs to a group of cases of pernicious anæmia with enlarged spleen, and does not come in the category of chronic cases here considered.

Case V.—Male, aged thirty-eight years; seen first November 10, 1898. For nearly twelve years he had had recurring hemorrhages. He returned to the hospital in January, 1900. Dr. Cushing removed the spleen. He did well for ten days, and then had a severe, uncontrollable hemorrhage from the stomach, which proved fatal. On post-mortem there were found (1) a practically normal condition of the viscera, (2) moderate cirrhosis of the liver, and (3) œsophageal varices, from one of which the last bleeding had occurred. The spleen showed a condition of chronic hyperplasia. In this extraordinary case the enlarged spleen had existed for fourteen years, and he had had throughout the period recurrent hemorrhages.

NEW CASES.

CASE XVI. *Clinical summary: Enlarged spleen and marked pallor for nine years; four severe attacks of hæmatemesis; removal of spleen; uncontrollable hemorrhage; death.*[1]—Frederick G., aged thirty years; referred to me by Dr. W. W. Johnston, January 14, 1901. The patient had lived in Washington all his life. When a boy at school he had chills and fever. He has had no attacks within ten years. For years he has been pale. He has, however, been able to attend to his work, and has been active and energetic. He is married. In 1892 it was first noticed that he had an enlargement in the abdomen. This was recognized by Dr. Johnston and others to be the spleen. It had caused him no inconvenience except for an occasional attack of pain in the side. He has had four severe attacks of hemorrhage from the stomach—the first in November, 1896, the second in November, 1897, the third in August, 1900, and the fourth on December 17, 1901, from which he is just recovering. Dark and bloody stools were often noticed after the attacks. They were of great severity. In the one in November, 1897, he had repeated hemorrhages, and very nearly died. He did not recover for nearly five months. Apart from the hemorrhages, his health, on the whole, has been good. The appetite and digestion had been normal and the bowels regular. He has never had a high color, but has had a curious gray pallor, with slight, diffuse pigmentation, which has increased of late. His average weight has been 133 pounds. The spleen was enormous, almost filling the left half of the abdomen. The liver was not enlarged.

He was urged by Dr. W. W. Johnston to have the spleen removed, in which opinion I concurred, and he was admitted to the hospital for preparatory treatment. The blood showed red corpuscles, 3,300,000; white blood corpuscles, 2400; hæmoglobin, 30 per cent.; moderate poikilocytosis; no nucleated reds. Between February 14th and April 14th he gained thirty pounds in weight! The blood improved, rising gradually, until on April 5th the red blood corpuscles were 5,200,000 and the hæmoglobin 75 per cent. On April 15th Dr. Halsted operated. After ligature of the splenic vessels great difficulty was met with in controlling the hemorrhage from the large veins passing to the stomach—vasa brevia—some of which were as large as the little finger. He lost so much blood that death took place a few hours after the operation. There was no autopsy. The liver, seen at the time of the operation, was smooth, and did not look cirrhotic.

CASE XVII. *Clinical summary: History of malarial fever eighteen years ago; tumor of left side of eleven years' duration; in* 1898 *an attack of severe anæmia, with ascites; recovery; in* 1900 *a second attack, with jaundice, anæmia, and ascites; gradual recovery; in* 1901 *a third attack, with jaundice, ascites, profound anæmia; recovery.*—Minnie W., aged forty years, was first seen in 1898, when she was admitted to Ward O on August 3d (Med. No. 8864), with great swelling of the abdomen and anæmia. She had been a healthy woman, married, three children—the youngest eighteen years old. She has always lived in Baltimore. In 1890 she had chills and fever through the summer, and they recurred

[1] The surgical and pathological aspects of Cases IV., V., and XVI. will be considered in a separate paper by Drs. Cushing and Macallum.

for several years. She has noticed a hard mass in the left side of the abdomen since 1890. On the first admission, August 3d, there was no jaundice. She had a greatly distended abdomen, œdema of the ankles, and an extreme anæmia. The red blood corpuscles were 2,500,000; hæmoglobin, 47 per cent.; white blood corpuscles, 1500. There were no malarial parasites; no pigment in the blood. The dropsy subsided rapidly, and it was then found that the spleen reached 18 cm. from the costal margin. A differential count of 525 leucocytes gave small mononuclears 21, large mononuclears 5, polymorphonuclears 67, eosinophiles 2.6, transitionals 1.9. Two nucleated reds were seen. With iron, good food, and open-air treatment (eight to ten hours daily) she improved rapidly, and on September 30th she left the hospital, with the condition of the spleen unchanged, but with the red blood corpuscles at 3,500,000; white blood corpuscles, 2400; hæmoglobin, 53 per cent. The edge of the liver could be felt 3.5 cm. below the costal border, "soft and slightly tender."

Second admission August 10, 1900, with jaundice, anæmia, and ascites. The jaundice had come on about three weeks previously. She has been pretty well for two years, and had been at work. The abdomen measured 92 cm. She was anæmic. Red blood corpuscles, 3,800,000; white blood corpuscles, 2000; hæmoglobin, 65 per cent. The ascites quickly disappeared and the jaundice lessened. She had two transient attacks of fever. There were no parasites in the blood, and no pigment. She left the hospital November 10, with red blood corpuscles at 4,600,000; white blood corpuscles, 7000; hæmoglobin, 70 per cent. The liver reached 3 cm. below the costal margin in the nipple line, and was very tender.

Third admission September 30, 1901, with jaundice, moderate ascites, and anæmia. She had kept pretty well since last note. Two weeks before admission she had nausea and vomiting and a chill. With the exception of the deeper jaundice her condition was a good deal better than at the last admission. The abdomen was large and contained a good deal of fluid. The spleen reached 5 cm. below the navel, and the edge was 18 cm. from the costal border. Red blood corpuscles, 3,800,000; white blood corpuscles, 4200; hæmoglobin, 58 per cent. As the fluid reduced the liver could be felt just below the costal border in the nipple line, and I noted on October 4th the "edge can be distinctly felt; it is very hard and feels cirrhotic." The jaundice was marked, and there were dilated venules on the face. She again improved, and on October 26th the red blood corpuscles were 4,700,000; white blood corpuscles, 3000; hæmoglobin, 62 per cent. The spleen was unchanged. On October 5th a differential count of 500 leucocytes gave polymorphonuclears 80.6, small mononuclears 9, large mononuclears 5.8, transitionals 3.4, eosinophiles 1.2.

Case XVIII. *Clinical summary: Enlarged spleen first noticed fifteen years ago; attacks of abdominal pains; marked pigmentation; slight enlargement of the liver; jaundice and secondary anæmia; slight fever; marked improvement.*—A. L. W., aged thirty-three years; admitted December 27, 1901 (Med. No. 13,848), with jaundice and slight fever. Inflammatory rheumatism fifteen years ago; ulcers on the right leg afterward. Sixteen or seventeen years ago had chills and fever. He went to Mexico, and while there was jaundiced and sickly for eight or nine months. He returned from Mexico fifteen years ago, and the

doctors told him he had an enlarged spleen, which has persisted ever since. He has had gonorrhœa, but has not had syphilis. He has been a moderate drinker. He does not think the spleen has increased much in size since it was first noticed. He has been pale for years; he has had occasional attacks of pain, and often a sense of discomfort after eating. For some time he has been losing in weight and feeling badly. His normal weight is 145 pounds; on admission it was 127 pounds. He has lately had cough, with fever and sweats.

On admission Dr. McCrae made the following note:

"His color is striking; he is exceedingly sallow. There are numerous areas of pigmentation over the face and forehead; there is definite jaundice. The patient is sweating profusely; tongue slightly coated; gums and mucous membranes rather pale.

"*Thorax.* Well formed, rather rounded. Expansion good; seems equal. Percussion note clear throughout; everywhere hyperresonant. Breath sounds seem clear throughout.

"*Heart.* There is rather a diffuse impulse. Point of maximum impulse, fifth left interspace, 155 cm. from mid-sternal line. Cardiac dulness begins at third right, opposite fourth interspace; extends 3 cm. to right and 11 cm. to left of mid-sternal line. Impulse well felt; no thrill. At apex the first sound completely replaced by soft murmur, carried to axilla. In fourth interspace there is a suggestion of a sound. On passing upward the systolic bruit increases in intensity, reaching a maximum in aortic and pulmonary areas. It can be heard on both sides out to about the nipple line; is loudly heard over the vessels of the neck. In the third left interspace close to the sternum the systolic murmur has a very rough quality. The second sound everywhere is soft. No definite diastolic murmur is made out. In aortic area has a murmurish quality. Pulse 24 to quarter, of fair tension, regular, of suggestive collapsing quality; there is a quick rise. Pulse is not that of aortic stenosis.

"*Abdomen.* Slightly full; no special visible prominence; no rose spots; walls fairly soft. Spleen very readily palpable; extends 12 cm. from the left costal margin, and comes to within 4 cm. of the navel and 5 cm. of the left anterior superior spine. It is hard, slightly tender, and slightly movable. Liver apparently also enlarged; in median line the edge being 5 cm. above the navel, and in the right nipple line 4 cm. below the costal margin. In the right nipple line dulness begins at the fifth right and extends 12 cm.; in the mid-axillary line dulness begins at the fifth interspace. The patient's body not specially pigmented, though dark; no special pigmentation about the nipples.

"Hæmoglobin, 53 per cent.; red blood corpuscles, 3,026,000; white blood corpuscles, 6875. Differential count; Jenner stain. Red cells show marked poverty in hæmoglobin, marked variation in size, there being many microcytes, no macrocytes, some poikilocytosis. In counting 536 cells no nucleated reds seen. Count in general shows relative increase in mononuclear elements; polymorphonuclears, 55.96; large mononuclears, 29.85; small mononuclears, 11.19; transitionals, 2.23; eosinophiles, 0.37; mastzellen, 0.37."

For five days his temperature ranged between 100° and 101° F., and he had a soft friction murmur in the left axilla. He had a small quantity of sputum, which was repeatedly examined for tubercle bacilli, with negative results. He gradually improved, the jaundice lessened,

but there seemed to be an increase in the general pigmentaton of the skin. By February 1st the patient was very much better. On the 2d, red blood corpuscles, 3,600,000; hæmoglobin, 65 per cent.

He was discharged February 7th, still looking rather pigmented, but free from fever, and having gained six pounds in weight. The urine contained bile at first, but was otherwise normal. The spleen was unchanged.

II. Incidence of Enlarged Spleen with Anæmia.

While the combination seems to be not infrequent, yet cases reported in the literature as splenic anæmia are rare. Rolleston, in his recent paper,[1] states that he has been able to collect only thirty-seven cases. In February last I sent a circular letter to members of the Association asking for information on the subject, and for notes of unpublished cases. I am indebted to twenty-four physicians for notes of forty-five cases, which I have grouped as best I could. It was not always possible to classify the cases properly, as in some no information was given as to the duration of the disease.

1. *Acute Anæmia, Under One Year's Duration, with Enlarged Spleen*, 12 cases.

In none of the cases was there a history of malaria; the duration of the illness ranging from eleven weeks to twelve months. The size of the spleen was not always stated. In the case of A. O. J. Kelly and J. C. Wilson it was only two fingers' breadth below the costal border, but in the cases of Cary, Edwards, Blackader and Martin, and Rotch the organ was greatly enlarged. In eight of the cases the red blood corpuscles were below 2,500,000 per cubic millimetre. In the cases of Musser and Blackader the count sank below 1,000,000 per cubic millimetre. The hæmoglobin was relatively low in six cases, of normal proportion in two, plus in two, and not given in two cases.

The leucocytes were under 6000 per cubic millimetre in eight cases; in three of these, below 2500. In two they were about normal, and in only two above normal, in one 7000 per cubic millimetre, and in one 20,000 per cubic millimetre.

In some of these cases the history, course, and blood condition suggest progressive pernicious anæmia. Case XIII., reported in my first paper, had, as I then remarked, many of the features of this disease. She returned (as noted in the early part of this article), and died with all the features of a pernicious anæmia plus great enlargement of the spleen. This group is of unusual interest, and brings up the question of the frequency of enlarged spleen in pernicious anæmia. Hunter[2] says "in a certain number of instances the spleen has been found enlarged, this condition being even recognizable during life." He mentions a number of cases reported by different observers; the largest mentioned "was in a case reported by Wilks (500 grammes). In 4 cases of his own the

[1] Clinical Journal, 1902.

[2] Pernicious Anæmia (monograph), 1901.

spleen weights were 19 ounces, 11 ounces, 10 ounces, and 13 ounces." In a great majority of the cases the spleen is either described as normal or no mention is made of the condition at all. Cabot[1] notes enlargement in 13 of 110 cases; Billings[2] in 5 of 20 cases. Among 40 cases from my wards, reported by McCrae,[3] "the spleen was felt in only 6 cases, and in none of them was the enlargement at all marked, it being noted that 'the spleen was just felt.'"

2. *Chronic Anæmia, with Enlarged Spleen*, 26 cases.

Eighteen of these were in males. The duration of the disease is most interesting: eleven years, 1 case; nine, 1; eight, 1; seven, 3; six, 2; five, 1; three, 2; four, 1; two, 3; between one and two years, 3; in 1 doubtful—"many years." In 9 of the cases the disease had lasted for more than five years; in 7 the duration was unknown. Hæmatemesis occurred in 9 cases, jaundice in 4 cases, ascites in 5, and in 7 cases the liver was enlarged. Several of the cases had been regarded as Banti's disease, or the terminal stage of anæmia splenica.

In only 7 of the cases were the red blood corpuscles below 2,500,000 per cubic millimetre. In 22 cases the hæmoglobin percentage was relatively low, in 3 it was normal, and in 1 it was not given. In 13 cases the leucocytes were below 5000 per cubic millimetre. In a case of Vickery's they were only 650 to 700 per cubic millimetre, and in Peabody's case they were only 800 per cubic millimetre, and the highest of several counts in this case was 1400. In 3 cases they were above 7000 per cubic millimetre, and in 9 cases they ranged from 5000 to 7000 per cubic millimetre.

3. *Simple Splenomegaly*, 2 cases.

Two cases were returned as simple or primitive splenomegaly. In Dr. Herrick's case the normal red count and the relatively low hæmoglobin, with a history of ill-defined symptoms for five years, suggest the early period of splenic anæmia. In Dr. Martin's case the enlarged spleen was found after an accident in which the man was knocked breathless. He vomited dark material. The spleen has gradually increased in size. There is practically no anæmia.

There were three cases difficult to classify, and in two cases other diseases were presented—cirrhosis of the liver and sarcoma of the spleen. The cases are given in an appendix in the *Transactions of the Association of American Physicians* for this year.

III. Anæmia Splenica Chronica.

Definition. *A chronic affection, probably an intoxication of unknown origin, characterized by a progressive enlargement of the spleen which can-*

[1] The American Journal of the Medical Sciences, 1900, p. 1.
[2] Journal of the American Medical Association, 1902.
[3] Ibid.

not be correlated with any known cause, as malaria, leukæmia, syphilis, cirrhosis of the liver, etc. (*primary splenomegaly*); *anæmia of a secondary or chlorotic type* (*leucopenia*); *a marked tendency to hemorrhage, particularly from the stomach; and in many cases a terminal stage, with cirrhosis of the liver, jaundice, and ascites* (*Banti's disease*). It seems probable that the conditions separately described in the literature as primitive splenomegaly, splenic anæmia, splenomegalic cirrhosis of the liver, or Banti's disease are stages of one and the same malady. Let me first give a brief analysis of the cases which have been under my care which conform to the above definition. I have cut out Cases I. and II. of my first series, as they were seen long ago (1879), though both patients had enlarged spleen and hæmatemesis; but I am uncertain about the duration and etiology. Case XIII. I have also discarded as probably progressive pernicious anæmia with greatly enlarged spleen. This leaves a group of fifteen cases seen within the past ten years; all have been carefully studied, and the full report of the blood condition will be found in the *Edinburgh Medical Journal*, May, 1899, and in THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, January, 1900, and in the present paper.

ABSTRACT OF FIFTEEN CASES.

CASE III.—Male, aged thirty-five years; duration twelve years. Enormous spleen; recurring attacks of hæmatemesis and melæna; pigmentation of the skin; death after an attack; no cirrhosis of the liver. Blood count lost.

CASE IV.—Male, aged thirty-three years; duration ten years. Recurring attacks of hæmatemesis and melæna; enormous spleen; pigmentation of the skin; removal of the spleen; liver not cirrhotic; recovery. Red blood corpuscles, 3,000,000; hæmoglobin, 25 per cent.; leucocytes, 2800.

CASE V.—Male, aged forty years; duration thirteen years. Recurring attacks of hæmatemesis; occasional melæna; enormous spleen; grayish-brown pigmentation of the skin; slight ascites; removal of the spleen; liver moderately cirrhotic; death from rupture of œsophageal varix. Red blood corpuscles, 4,000,000; hæmoglobin, 30 per cent.; leucocytes, 6500.

CASE VI.—Male, aged twenty years; duration eleven years. Onset with hæmatemesis; pigmentation of the skin; spleen very large. Red blood corpuscles, 2,187,000; leucocytes, 12,497.

CASE VII.—Male, aged forty years; duration two years. Enormous spleen; recurring cutaneous hemorrhages; remarkable pigmentation of the skin. Red blood corpuscles, 4,816,000; hæmoglobin, 55 per cent.; leucocytes, 5000.

CASE VIII.—Female, aged fifty-six years; duration three years. Spleen very large; no hemorrhages; no pigmentation. Red blood corpuscles, 3,600,000; hæmoglobin, 60 per cent.; leucocytes, 3000.

CASE IX.—Male, aged fifty-eight years; duration six years. Spleen very large; recurring ascites; no hemorrhage; no pigmentation;

enormous ascites; no cirrhosis of liver; death. Red blood corpuscles, 4,788,000; hæmoglobin, 60 per cent.; leucocytes, 5200.

Case X.—Male, aged thirty-nine years; duration doubtful—more than three years; hæmatemesis, melanoderma, and leukoderma; spleen greatly enlarged. Red blood corpuscles, 4,128,000; hæmoglobin, 45 per cent.; leucocytes, 2800.

Case XI.—Male, aged fifty-seven years; duration two years. Spleen greatly enlarged; no hemorrhages. Red blood corpuscles, 2,500,000; hæmoglobin, 37 per cent.; leucocytes, 3000.

Case XII.—Male, aged forty years; duration (now) four years. Greatly enlarged spleen; recurring hæmatemesis; ascites; recovery. Red blood corpuscles, 4,208,000; hæmoglobin, 45 per cent.; leucocytes, 4000.

Case XIV.—Male, aged thirty-five years; duration (now) four years. Hemorrhage from kidneys; no malaria; greatly enlargd spleen; marked pigmentation of the skin. Red blood corpuscles, 3,856,000; hæmoglobin, 55 per cent.; leucocytes, 4500.

Case XV.—Male, aged forty-three years; duration eight years. Very large spleen; recurring hæmatemesis. Red blood corpuscles, 4,270,000; hæmoglobin, 45 per cent.; leucocytes, 2500.

Case XVI.—Male, aged thirty years; duration ten years. Recurring hæmatemesis; grayish-brown pigmentation of the skin; removal of spleen; no cirrhosis of liver; death. Red blood corpuscles, 3,300,000; hæmoglobin, 30 per cent.; leucocytes, 2400.

Case XVII.—Female, aged forty years; duration ten years. Recurring attacks of acute anæmia, with jaundice and ascites; enormous spleen; no hemorrhages. Red blood corpuscles, 3,500,000; hæmoglobin, 53 per cent.; leucocytes, 2400.

Case XVIII.—Male, aged thirty-three years. Duration of enlarged spleen fifteen years, organ greatly enlarged; liver also enlarged; slight jaundice; marked pigmentation of the skin; no hemorrhages. Red blood corpuscles, 3,326,000; hæmoglobin, 53 per cent.; leucocytes, 6875.

As in the cases collected by Rolleston, the *sex* in my series shows a great prevalence among males—thirteen to two. All of the cases were in adults, chiefly in young adults; in only one (Case VI.) had the disease begun in childhood.

There is nothing in the *etiology* of the cases to throw any light on the causation. The question of *malaria* naturally arises, considering the locality in which I practice. There was history of malaria in five cases. In three of these (aged forty, fifty-six, and thirty years) the infection was in childhood. In only two (Cases XVII. and XVIII.) had the infection occurred in adult life—one twelve years before onset of illness, the other eighteen years before. The locality has nothing to do with the number of cases observed; only five cases came from Maryland, four of which were from the city of Baltimore. The others came from New York, Pennsylvania, Illinois, Massachusetts, West Virginia, North Carolina, South Carolina, Canada, and Jamaica.

Heredity has played no part in my cases, but Brill[1] has reported three cases in one family. One girl died, aged nine years, with enlargement

[1] The American Journal of the Medical Sciences, April, 1901.

of the spleen. The description of the other two cases leaves no doubt, I think, that they belong to the disease under discussion. Case III., with the peculiar pigmentation, the tendency to hemorrhages, and the type of anæmia present, corresponds exactly with chronic splenic anæmia. Bovaird[1] has described a similar condition in two sisters; a sister of Collier's[2] patient died with enlarged spleen, while C. Wilson[3] has reported a family in which in three generations six members had enlarged spleen. It is quite possible that all of these cases belong in the category of chronic splenic anæmia.

SYMPTOMATOLOGY. 1. *The Remarkable Duration of the Disease.* Among disorders of the blood or blood-making organs anæmia splenica is characterized by an extraordinary chronicity. In some of the cases in my series the disease had lasted more than twelve years. Rolleston reports a case of twelve years' duration, beginning in the eleventh year, the condition remaining throughout very much the same, except that during the last three years of life there was recurring hæmatemesis. Senator and others have noted this peculiarity. An extraordinary illustration I saw last winter in New York with Dr. Walter James, who will report the case in full. The patient had had an enlarged spleen, with anæmia of varying intensity, for at least twenty-five years. He died at last in a profound anæmia, with ascites. Gaucher's case of splenic enlargement existed for twenty-five years. In my series of fifteen cases, in seven the duration of the disease was more than ten years, and in eleven more than four years.

In ten of the twenty-six cases of chronic splenic enlargement, with anæmia, under the care of my colleagues in the Association, the disease had lasted more than five years. It is strange how slight may be the inconvenience, even with a spleen extending below the navel. A majority of my patients were active business men, and, as in Cases III. and XVI., the chief trouble was the recurring hæmatemesis and the protracted up-hill convalescence after the attacks.

2. *The Splenomegaly.* There are many conditions in which the spleen may be enlarged for months or years, sometimes without any apparent injury to health. I have had a group of cases of moderate enlargement of the spleen in women, without obvious cause and without marked anæmia, in which the discomfort of the movable organ was the chief complaint. Two of these cases have remained well for years, having had the organ "packed" into position. Among the dark-skinned emigrants from southern and eastern Europe and from Armenia moderate enlargement of the spleen is not uncommon—a point noted by Cabot in the discussion of this paper. It may be a manifestation of latent paludism.

[1] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, October, 1900.
[2] Pathological Society Trans., vol. xlvi.
[3] Clinical Society Trans., vol. xxiii.

In the very large group of cases of splenomegaly, with secondary anæmia:

(*a*) The cause is usually apparent—malaria, tuberculosis, rickets, or syphilis—particularly in children, in whom any state of malnutrition, if protracted, may be associated with enlargement of the spleen.

(*b*) The anæmia and splenomegaly usually yield to appropriate treatment; at all events there is not the remarkable chronicity.

(*c*) The spleen in this group rarely reaches the colossal size seen in chronic splenic anæmia.

(*d*) The sequences so characteristic of splenic anæmia are not seen.

(*e*) While the blood shows the features of a secondary anæmia there is rarely the exaggerated chlorotic type, and leucocytosis is more common than leucopenia.

There are many gaps in our knowledge, and it is difficult to assign to individual cases their proper places. It may not always be possible to speak definitely. For example, in the case of James P., aged four years, sent by Dr. Rotch (No. 12, acute cases), with a large spleen and a marked anæmia, with leucopenia of two months' duration, where shall we classify it? or a case, sent by Cabot, of a child aged seven months, duration of illness not stated, with red blood corpuscles 3,200,000; hæmoglobin, 25 per cent.; leucocytes, 36,800, and nucleated red blood corpuscles 6190 per cubic millimetre? The anæmia is more or less acute, the splenomegaly moderate, and the blood condition may be very variable. On the other hand, many of the cases in children conform to the definition above given of chronic splenic anæmia. Another case of Rotch's (No. 18 in chronic series): At the age of three years the spleen and liver were large, the anæmia was marked; nine years later the spleen was enormous, the liver still enlarged, the anæmia pronounced, and the skin was pigmented.

The special feature of the enlarged spleen in chronic splenic anæmia is the size, which is unequalled in any other disease, except, perhaps, leukæmia. The abdomen may be enormously distended, and the organ may not only occupy the left side, but may curve upon itself and pass across to the right iliac fossa and the right flank. The notches may be directed upward, as in one of Collier's cases which I saw with him at the Radcliffe Infirmary, Oxford, in which the border of the spleen and the notches were between the navel and the ensiform cartilage. The average weight in twelve cases collected by Rolleston was sixty-one ounces. In Bovaird's case the organ weighed twelve and one-half pounds. The mechanical discomfort may be considerable, though as a rule there is very little pain unless perisplenitis be present, in which case a friction may be felt or heard. In Rolleston's case a *bruit de diable* was heard over the organ.

Many of the cases reported in the literature as primary or primitive

splenomegaly come under the definition of the disease as given above. In the chronicity (eleven and fifteen years and thirteen years) and in the general features the cases of Brill and of Bovaird conform to chronic splenic anæmia.

3. *Hæmatemesis* is a remarkable feature of the disease. Eight of my patients had attacks of vomiting of blood. In Cases I. and II. (which I have discarded from my series as seen in 1879 as deficient in certain details) the hemorrhages were most profuse. I have never seen such enormous losses of blood as in Case II. In the nineteen cases communicated by members of the Association, hæmatemesis occurred in seven. In a large proportion of the cases the hemorrhage is due to conditions associated with the enlarged spleen, not to accompanying cirrhosis of the liver. In Cases IV. and XVI. of my series the spleen was removed, and at the operation the liver was seen to be normal. In Case III. it was not cirrhotic post-mortem. It is easy to understand this splenic origin, as 40 per cent. of the blood from the stomach passes by the vasa brevia to the splenic veins. (Mall and Krauss.) Watson gave a mechanical explanation (which I have quoted in my first paper) of the bleeding. The source of the blood may be (*a*) a general diapedesis from the gastric mucosa. This is doubted by some writers, but on several occasions I have not been able to find, after a most careful search, either minute erosions of the mucosa or ruptured veins in the œsophagus, and there seems to be no other explanation; (*b*) small erosions of the gastric mucosa; (*c*) rupture of a varicose vein of the œsophageal plexus, which was the cause of death in Case V. after removal of the spleen. The recurring profuse bleedings may very often be from this source, considering the intimate relation between the veins of the fundus of the stomach supplying the *vasa brevia* and those of the cardiac orifice and the œsophagus; (*d*) Rolleston suggests that the large wandering spleen may pull on the gastrosplenic omentum and give rise to torsion of the veins, or cause a kink in the splenic vein, and so induce intense venous engorgement of the stomach.

With the exception of the chronic hemorrhagic form of the peptic ulcer there is no known condition in which hæmatemesis may occur for so many years. In Preble's[1] study of gastro-intestinal hemorrhages in cirrhosis of the liver, in five of the thirty-five cases in which œsophageal varices were found the hemorrhages had occurred at intervals varying from a few months to five years.

Hemorrhage from other sources is less frequent. Epistaxis may recur at intervals; retinal hemorrhages, bleeding gums, menorrhagia, and hæmaturia have been recorded. Purpuric attacks, as in Case VII. of my series, may occur.

[1] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, January, 1901.

4. *Anæmia.* Even in well-defined cases the anæmia may be slight. As in locomotor ataxia there may be no ataxia, so in anæmia splenica there may be no corpuscular anæmia—a point which may be urged against the use of these names. Take, for example, Case XVI., here reported. Prior to the operation there was no anæmia of corpuscles, which were 5,200,000 per cubic millimetre, but he was still pallid and had only 75 per cent. of hæmoglobin, and there was not the slightest change in the spleen; yet he presented a most typical picture, and anyone who had seen Cases III., IV., and V. could have recognized at a glance that the case belonged, with them, to a separate clinical group, quite as definite as leukæmia or Addison's disease. Very few of the patients will be found to have a normal amount of hæmoglobin; they are constantly "off color."

There is nothing peculiar or distinctive in the anæmia, which is of the secondary or chlorotic type.

(*a*) *The corpuscular anæmia* is of a moderate grade. Of the forty-one cases of my series the average was 3,425,000 per cubic millimetre. The lowest blood count was 2,187,000; the highest count was 5,200,000, in the patient just referred to.

(*b*) *The low hæmoglobin* is an interesting feature, and rather more striking than in other secondary anæmias. It is certainly rare, except in chlorosis, to find a patient with obvious anæmia and a blood count (corpuscles) normal or even, as in Case XVI., above normal. The average of thirteen hæmoglobin counts was 47 per cent.

(*c*) *Leucocytes.* Immediately after a profuse hemorrhage, or in a terminal affair, there may be a leucocytosis, but, as a rule, there is a leucopenia. Of fourteen cases the average leucocyte count was 4520 per cubic millimetre. If we leave out Case VI., admitted shortly after a severe bleeding, with a leucocytosis of 12,500, the average of thirteen cases—in one of the series (III.) the blood count was mislaid—was 3850 per cubic millimetre.

In the extreme anæmia which may come on at the close there may be marked poikilocytosis, with nucleated red corpuscles, etc. There has been nothing characteristic in the differential count of the leucocytes.

5. *Pigmentation of the skin* is a common event in the very chronic forms, having been present in eight of my cases. A majority of these presented the usual bronzing of the skin, diffuse in character, and resembling that seen in Addison's disease, though rarely so intense. In some it was a curious steel-gray staining of the skin, of a very peculiar character, suggesting rather argyria than the usual form of melanoderma. In some cases it was patchy and associated with areas of leucoderma.

Pigmentation of the skin seems to be a common feature in the long-standing cases, and has been commented upon by Brill, Bovaird,

Frederick Taylor, and others. It is of special interest in connection with the melanoderma of hæmochromatosis (bronzed diabetes) and of Hanot's cirrhosis. In Case XIV. of the series a portion of the skin did not show the ochre-brown pigment such as is present in hæmochromatosis. It is to be borne in mind that arsenic is used largely in these cases, and it is quite possible that to it in part may have been due the dark color of the skin. In no case were there keratoses.

6. *Hepatic Features.* The mutual relations of diseases of the spleen and liver are well illustrated in splenic anæmia. While a majority of the cases present no symptoms of disturbed action of the liver, and in a few the occurrence of ascites, even when the liver is normal, suggests cirrhosis, there is a third group in which the hepatic features so predominate that cirrhosis of the liver is at once suspected. Hæmatemesis is a splenic, not an hepatic, feature of the disease. Cases IV. and XVI., in which the hemorrhages had occurred for many years, presented at the time of operation a normal liver. Case IV. was alive and well (having had no recurrence of the hemorrhage) nearly three years subsequently. While hemorrhage from the stomach may be a very early, indeed, the very first, symptom of cirrhosis of the liver, it is most unusual to have recurrences over long periods, as in the cases recorded in this series. Even in the more chronic type of cirrhosis—Hanot's variety—hæmatemesis is not so special a feature as in splenic anæmia. In the later stages of the disease the cirrhosis of the liver, if present, as in Case V., may aggravate the conditions favoring hemorrhage. In my series hepatic features have not been very marked.

Ascites occurred in four cases. In Case V. it was slight and associated with œdema of the ankles. The patient had had shortly before readmission a series of bleedings. At the operation, and ten days subsequently at autopsy, slight cirrhosis of the liver was found. In Case XVII. ascites was present at the time of the admissions, August 3, 1898, August 10, 1900, and September, 1901. In each instance it disappeared with the general improvement. In the second and third admissions there was jaundice. The liver was slightly enlarged and felt cirrhotic. In Case XII. there was no dropsy when I saw him; six weeks before six quarts were drawn off. Dr. Vickery writes that he had been tapped again. The liver was not enlarged. In Case IX. there was ascites in 1895, again in 1897, and a third time in his final illness, in the spring of 1898. The liver could be felt a little below the costal border, but at the post-mortem there was no cirrhosis

In the series of cases of anæmia, with enlargement of the spleen, sent by my colleagues, ascites was present in the cases of McPhedran, Edes, Atkinson, Sears, and Cabot; in two of the cases in association with jaundice.

Jaundice was present in only two cases in my series and in four in the association series.

State of the Liver. In eight cases the liver was of normal size. In Cases IV. and XVI. the organ was seen to be smooth and natural looking at the time of operation. In Cases III. and IX. it was normal post-mortem. In six cases it was slightly enlarged; in no case was the organ large and hard, as in forms of hypertrophic cirrhosis. In one case it was reduced in size; in only one (Case V.) was cirrhosis of moderate grade found post-mortem. In seven of the cases in the association series the liver was enlarged.

Relation of the Cirrhosis of the Liver to the Enlarged Spleen. Splenomegaly and cirrhosis of the liver are associated in the following conditions:

1. *Atrophic Cirrhosis of the Liver.* So constant is moderate enlargement of the spleen that in doubtful cases it is an important help in diagnosis. The organ is not often very large, rarely reaching to the navel. That it is due to the chronic passive congestion is shown by the remarkable reduction in size which may follow an attack of hæmatemesis. There is a moderate hyperplasia and often a perisplenitis. Parkes Weber suggests that the enlarged spleen may be due in part to a toxæmia.

2. *Syphilis of the Liver.* Both liver and spleen may be involved in amyloid degeneration, but the cases in question are gummata of the liver, with consecutive contraction. The spleen may reach a very large size. A remarkable congenital case, in a girl twenty-one years of age, occurred some years ago in my wards,[1] in which, in addition to the big spleen and syphilitic liver, there was a high degree of leucocytosis.

In my previous paper on splenic anæmia I have reported two other cases, and have called attention to the liability of error. In one of the histories sent by Dr. Musser the patient, aged forty-five years, had had syphilis of the brain. In 1898 and 1899 he had jaundice, with great enlargement of the spleen and liver, hemorrhages from the stomach and bowels, and moderate anæmia. In Coupland's case[2] an enlarged spleen was removed, and two years later the patient died with hæmatemesis and ascites; the liver was found to be syphilitic. When we recognize more fully the great frequency of syphilis of the liver[3] and learn the extraordinary diversity of its clinical features we shall find, I think, a very interesting group of cases characterized by irregularly contracted liver, big spleen, and anæmia.

[1] Johns Hopkins Hospital Bulletin, vol. ii. [2] British Medical Journal, 1896, vol. i.
[3] See recent papers by Einhorn, Medical Record, 1901, and Stockton, Journal of the American Medical Association, 1902, vol. ii.

In both the alcoholic and syphilitic cirrhosis the liver, as a rule, is small, and *the splenomegaly follows and depends, in great part at least, on the condition of the liver.*

3. *Hæmochromatosis.* This remarkable and most obscure affection is characterized by a chronic curve, a gradual deposition of an iron-containing pigment in the organs and in the skin (leading to pigmentation), a progressive enlargement of the spleen, hypertrophic cirrhosis of the liver, sclerosis of the pancreas, and, finally, diabetes—the bronzed diabetes of the French. Anschutz[1] and Opie[2] regard the affection as a chronic toxæmia leading to hæmolysis, with gradual deposition of blood pigment in the organs (leading to sclerosis) and in the skin. There may be a marked tendency to hemorrhage (purpura). In the cases I have seen the spleen has not been enormously large,[3] and the condition is one in which *the splenomegaly and the cirrhosis of the liver go hand-in-hand*, both apparently due to the same cause.

Anæmia, so far as I can learn, has not been a special feature of the cases. It is of interest to note that in the case which was reported by H. A. Hare as Banti's disease, and which had been under the care of Musser and J. C. Wilson, the patient, who had been ill for seven years, had a very large spleen, moderately enlarged liver, anæmia, and diabetes. No mention is made of pigmentation of the skin.

4. *Other Forms of Cirrhosis.* Apart from the alcoholic and syphilitic varieties, there is a large group of cases in which the disease occurs chiefly in the young, usually the hypertrophic form, and in association with great enlargement of the spleen.

(*a*) *Hanot's cirrhosis*, the best known of these varieties, is a very chronic enlargement of the liver occurring in young persons, sometimes as a family form, not associated with the abuse of alcohol or with malarial or syphilitic infection. The spleen is enlarged, but not of very great size in proportion to the liver. There is a chronic jaundice of varying intensity, a marked tendency to hemorrhage, but not specially to hæmatemesis, and very often a terminal *icterus gravis.* Rarer features are bronzing of the skin, a marked leucocytosis, and fever. Ascites does not occur (?). The relation in time of the hepatic enlargement and the predominance of the biliary symptoms from the outset are characteristic features. The lesions are those of a biliary cirrhosis.

(*b*) There is a *simple cirrhosis* of the liver in children, without great enlargement of the liver, moderate splenomegaly, and a clinical picture almost identical with that of the disease in adults. Ascites is a prominent feature. Some of the cases have been of alcoholic origin, but in

[1] Deutsches Archiv für klin. Med., 1899, Band lxii.
[2] Opie. Journal of Experimental Medicine, vol. v.
[3] British Medical Journal, 1899, vol. ii.

a majority I think the starting point has been in the changes which have followed one of the fevers of childhood. The condition is certainly very different from Hanot's cirrhosis, and very different, too, from the third type, (*c*) *splenomegalic cirrhosis*, the form which specially concerns us here on account of its relations with splenic anæmia, and must be discussed as a separate section.

5. *Splenomegalic Cirrhosis of the Liver.* After lasting for some time, splenic anæmia may be followed by cirrhosis of the liver. It was the merit of Banti to call attention to this sequence. The splenomegaly may exist for a long period of years without leading to cirrhosis of the liver, as illustrated in Cases III. and IV. of my series. In Case V., after a period of between thirteen and fourteen years, the organ was only moderately cirrhotic. The enlargement, in adults at least, is not very great, and the splenic features dominate the case throughout, and the ascites and hæmatemesis, as I have insisted, do not necessarily indicate that the liver is involved.

Can we bring into this category the remarkable group of cases in children, particularly the family form of splenomegaly, which corresponds in so many features with chronic splenic anæmia? Take, for example, the case reported by Frederick Taylor.[1] The lad, aged thirteen years, had for six years an enlarged spleen, with jaundice and enlarged liver. There were anæmia, melanoderma, hemorrhages, and clubbed fingers. Post-mortem the spleen weighed eighty-seven and a half ounces, and the liver, only forty ounces in weight, was rough and nodular. The case is reported as one of splenomegalic cirrhosis. Bovaird's case, already referred to, was one of two sisters affected. At the age of sixteen years, thirteen years after the onset, there was marked anæmia, no jaundice, enormous spleen, moderate enlargement of the liver, and melanoderma. The spleen weighed twelve and a half pounds; the liver, sixty-eight ounces, was cirrhotic. In Rotch's case the lad, aged twelve years, had had a big spleen for nine years. When three years old the spleen and liver were enlarged, and there was anæmia. Nine years later the spleen was enormous, reaching to the pelvis; there was pigmentation of the skin and extreme anæmia, without leucocytosis. In the cases of Edes (No. 8) and Vickery (No. 12), also of long duration in children with enormous spleens—ascites in the one case and hæmatemesis in the other—the liver was not enlarged.

Some of these are undoubtedly cases of splenic anæmia in childhood. The truth is, we need a very careful study of this group of cases before we can speak of them with any certainty. The cases are singularly chronic, and pass from one physician to another. The relation in time

[1] Guy's Hospital Reports, vol. liv.

of the hepatic and splenic lesions, the forms of hypertrophic cirrhosis of the liver in children, the relation of the family variety to the others, the state of the liver in the cases of primary splenomegaly, the condition of the blood, the relation of the cases to hæmochromatosis and to Hanot's cirrhosis—these are some of the questions awaiting solution. I have purposely refrained from using the terms introduced of late years by our French colleagues, whose studies in cirrhosis of the liver have been so important. The long-sounding names simply express the plain fact that the cirrhosis of the liver may precede (as in portal cirrhosis), accompany (as in hæmochromatosis), or follow (as in splenic anæmia) the splenomegaly. For the last group the term splenomegalic cirrhosis is allowable; but, as Dr. Frederick Taylor says, it is devoutly to be hoped that "we may be delivered from the cumbrous and unwieldly nomenclature which has been suggested for temporary use by our foreign *confrères*."

Pathology. The morbid anatomy throws very little light on the origin of this remarkable disease. Two conditions have been described in the spleen: 1. A fibrosis and hyperplasia, with atrophy of the pulp and a hyaline degeneration of the Malpighian bodies;[1] and with this description Dr. W. G. McCallum tells me our cases (IV., V., and XVI.) correspond, with certain minor differences. 2. On the other hand, a very remarkable change has been found in certain cases of splenomegaly; cases which, as I have said, agree in every clinical particular with the definition of the disease above given. The normal texture is largely replaced by fibrous tissue and large endothelial cells with clear protoplasm containing two or more nuclei, and among them giant cells. The condition is beautifully shown in the illustration in Bovaird's article. No wonder that Gaucher described it as primary endothelioma, although the spleen had been enlarged twenty-five years. The same structure has been described by Picou and Ramond, Collier, Harris and Herzog, and Rolleston. "It has been suggested by Bovaird that the proliferated endothelial cells eventually form fibrous tissue, and, though Harris and Herzog do not support this, the microscopic appearances certainly are compatible with this view. It is perhaps more probable that the fibrous hyperplasia goes on at the same time as the endothelial proliferation, and is due to the same cause, viz.: a chronic intoxication. The fibrous tissue of the organ contains pigment granules of hæmosiderin and hæmatoidin. . . . In some recorded cases fibrosis and atrophy of the pulp and Malpighian bodies have been the only changes described. It is perhaps possible that in such cases the change has progressed, as it may do, in lymphadenoma to fibrosis and disappearance of the endothelial proliferation" (Rolleston). A point to be emphasized

[1] Banti. Zeigler's Beiträge, Band xxiv.

in favor of the view that these two changes of endothelial proliferation and fibrous hyperplasia are part of the same process is the identity of the clinical course in cases in which one or other of the changes has predominated. In Bovaird's patient the splenomegaly had lasted thirteen years; there was marked pigmentation, a secondary anæmia, and moderate sclerosis of the liver. In Rolleston's case the enlarged spleen had existed twelve years, and, as already stated, in Gaucher's patient twenty-five years.

The true nature of the disease is unknown. It is probably a chronic toxic rather than an infective process, but of the character and the source of the poison we are ignorant. Naturally, with the prevalence of theories of autointoxication, the origin has been sought in the intestinal tract—among the *fermenta imaginaria*, of which Glisson speaks in the section *de Flatu* of his celebrated *Tractatus de Ventriculo et Intestinis*. Harris and Herzog suggest that a chronic hæmolysis is caused by an enzyme manufactured by the endothelial cells of the spleen, but this does not explain the cause of the splenic changes. That the spleen is a most important factor in the disease is shown by the cure which has followed its removal, as though the organ was the seat of the manufacture of some poison; but all this is theory.

NOMENCLATURE "What 's in a name?" may well be asked of the disorder under discussion, to which an unusual number of labels have been attached. The all-important matter is to define as accurately as possible the condition named, according to the good rule laid down by Socrates: "Now, I have no objection to your giving names any significance that you please if you will only tell me what you mean by them."[1] If our knowledge does not permit to give a name according with the etiology of the disease, the rule should be to pick the one which seems least objectionable, taking priority and usage into account. To me splenic anæmia seems a less objectionable term than *splenic pseudoleukæmia*, *splenic lymphadenoma*, *splenic cachexia*, *primitive splenomegaly*, or *Banti's disease*. So far as we know, the primary involvement is of the spleen, though the anæmia and the enlargement of the organ may both depend on a common, unknown factor. The name certainly expresses the two most constant features of the affection, though the anæmia is not necessarily present throughout. A serious objection is that the term has been used in a generic sense, as under anæmia splenica several diseases have doubtless been described; but the condition here described has features so remarkable and definite that to restrict the term to it seems advisable, with the qualifying addition of the word *chronic*. The protracted course of the disease is one of its most extraordinary peculiarities, and serves to separate this group from the acute

[1] Plato's Charmides (Jowett's Plato, vol. i. p. 21).

anæmias with enlargement of the spleen. Usage, too, should count, and it is something that the name should have been introduced by a great clinical physician, Griesinger, and has been adopted by such men as Strümpell, Senator, Coupland, Rolleston, and others.

The name *primary* or *primitive splenomegaly* has the advantage of neutrality or indifference in not suggesting any theory of origin, and there is no objection to its use in designating cases—such as those reported by Herrick, Martin, and others—in which the enlarged spleen constitutes the only manifestation. *Banti's disease* is simply chronic splenic anæmia plus features of cirrhosis of the liver, which represent a terminal stage in the disease. Banti's merit consists in calling attention to this important aspect; but, after all, these secondary changes in the liver are somewhat rare, and, as my records show, the hemorrhages, ascites, and even the jaundice may be present without existing cirrhosis.

Treatment. Since my first paper there has been a notable contribution made to the treatment of splenic anæmia in the study, by Harris and Herzog,[1] of the results of splenectomy. Of nineteeen cases, in fourteen recovery followed; in one the result was not given. In three of my patients, as already stated, the spleen was removed. In Case IV. (operated on by Dr. Cushing) the man, when heard from last, three years after the operation, remained well. This man had had at intervals of a year, for ten years, attacks of hæmatemesis. In Case V. (operated on by Dr. Cushing), in which the hemorrhages had recurred for more than fourteen years, death occurred on the tenth day from rupture of an œsophageal varix. In Case XVI. (operated on by Professor Halsted) the patient died of uncontrollable hemorrhage from the large veins passing between the stomach and the spleen. Recurring hæmatemesis, the most serious event in the disease, and, as I have insisted, usually of splenic origin, is the most important indication for operation

Conclusion. A growing clinical experience should give a sort of miniature picture of the general clinical experience of the profession. Few of us see all the aspects of any disease; few of us recognize all the aspects of the diseases we see; but all of us can try to correlate our own observations with the facts presented by our colleagues, and this is what I have attempted in these papers on splenic anæmia. The conclusion to which I have been led by the study of a remarkable group of cases is that—

From among the conditions with which anæmia and enlarged spleen are associated a well-defined disease may be separated conforming to the definition above given, and which may be called chronic splenic anæmia.

[1] Annals of Surgery, July, 1901.

THE ROLE OF THE TOXINS IN INFLAMMATIONS OF THE EYE:

BEING AN ESSAY TO WHICH WAS AWARDED THE BOYLSTON PRIZE.

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The investigations of Sattler, von Michel, Fick, Weeks, and others have shown that bacteria are constantly present in the normal conjunctival sac, and that these bacteria are not always harmless. It is no uncommon thing to find either the micrococcus lanceolatus or the staphylococcus aureus in a conjunctiva which is, clinically speaking, normal, while Randolph's[1] investigations prove that the micrococcus epidermidis albus (Welch) is an almost constant inhabitant of the normal conjunctival sac.

The researches of Uhthoff and Axenfeld[2] show that the pneumococcus is the most important etiological factor in serpent ulcer of the cornea, and this affection is commonly spoken of nowadays as "pneumococcus ulcer." Such an ulcer usually presupposes two conditions—first, a break in the cor .eal epithelium; and, second, the presence of the pneumococcus, which, as I have said, is often found in the conjunctival sac.

And when I speak of the staphylococcus aureus I am reminded of the records of many unsuccessful cataract operations where failure was traced to the presence of this organism, which there were strong reasons for believing was not introduced into the conjunctiva through blunders in modern operative technique.

The micrococcus epidermidis albus has but slight pathogenic properties, and to this we owe it in large measure that so many eyes survive serious wounds, for this organism has been demonstrated as being generally present in the normal conjunctival sac. Abundance of evidence, then, is at hand to show that the healthy conjunctiva, like the healthy vagina and the healthy intestine, probably contains bacteria at all times.

On the other hand, we know that most inflammations of the conjunctiva are caused by the growth and multiplication, either in the conjunctiva or on its surface, of special bacteria. Trachoma, vernal catarrh, and phlyctenular conjunctivitis have all been thought to originate in special bacteria, and efforts to solve these problems have brought forth much that is valuable, but nothing definite. Personally, I feel quite certain of the parasitic origin of trachoma, but I doubt whether it can be shown that either of the other diseases has its own bacterium. But when we speak of serpent ulcer, acute contagious conjunctivitis or "pink eye," gonorrhœal ophthalmia, and subacute or

chronic conjunctivitis we no longer walk on debatable ground, but are in territory whose landmarks are well established, and at once we remember that serpent ulcer is caused by Fraenkel's pneumococcus, "pink eye" by the Koch-Weeks bacillus, gonorrhœal ophthalmia by the gonococcus of Neisser, and subacute or chronic conjunctivitis by the diplobacillus of Morax-Axenfeld.

These are only a few examples which show the relationship which bacteria bear to inflammations of the eye, and as ophthalmic literature of the past ten years is full of proof of this fact, it is unnecessary for me to multiply evidence of this character.

How do these, or in fact any organisms, produce inflammation of the conjunctiva? Either by acting as a foreign body—in other words, by irritating the conjunctiva—or by producing soluble substances, which in their turn act upon the cellular elements of the tissues. It is easy to see that there are decided objections to accepting the view that when organisms produce inflammation of the conjunctiva they do so by acting as foreign bodies, for in that case all organisms would be on pretty much the same footing when present in the conjunctiva, and they would always produce more or less irritation. Then, again, it would be difficult to explain how certain organisms produce more intense reaction than others, for, so far at least as size is concerned, there is no significant difference in the bacteria which we usually find in the conjunctival sac; and we know, too, that in the case of the very organisms which I have mentioned (as causing specific inflammation of the eye) they must have been a certain length of time in contact with the surface of the conjunctiva before the clinical symptoms of inflammation are visible. The mechanical hypothesis, then, if I may so term it, can easily be shaken; while the other hypothesis—the gist of which is that the inflammation results from the action of the poisonous products of the organisms upon the cells of the eye—rests upon a much firmer foundation.

It is evident, however, that we are beset with many difficulties when we attempt to prove this experimentally, for we know that the Koch-Weeks bacillus, the gonococcus, and the diphtheria bacillus are peculiar to man, and that these bacteria will produce little or no reaction in the conjunctiva of animals, because the medium is not the proper one for their growth. Heller[3] inoculated the conjunctiva of the newborn rabbit with a gonococcus culture, and claims to have found the organism living in the purulent secretion of the conjunctival sac twenty-four hours after the inoculation. I have repeatedly tried to get a reaction by introducing this organism into the conjunctival sac of the rabbit, but the result of the experiment was always negative, and even when a slight wound of the conjunctiva was made the reaction was very doubtful.

Morax and Elmassian[4] have repeated Heller's experiments, and have occasionally succeeded in getting his results. In order to get the desired reaction one must secure a very virulent race of gonococci—that is to say, the organism must have figured in a very severe case of gonorrhœa. One must introduce as much as possible of the culture (of twenty-four hours' growth) into the conjunctiva. The lids must then be either occluded with collodion or a thread passed through them, and this condition maintained until the next day. But even with conditions so favorable Morax and Elmassian failed to produce an inflammation which was comparable to the gonorrhœal ophthalmia of the human being; and as regards the organism itself, cover-slips gave most unsatisfactory information, while nothing grew from cultures made from the inoculated conjunctival sac.

From all this it would seem clear that it is impossible to produce with the gonococcus in the rabbit's conjunctiva a reaction similar to genuine gonorrhœal ophthalmia, and the same observation holds good for the diphtheria bacillus, the Morax-Axenfeld diplobacillus, and the Koch-Weeks bacillus.

Infectious bacteria produce inflammation in the conjunctiva not only by growing and multiplying in this region, but, in addition, by producing substances called toxins. Toxins, according to Armand Gautier,[5] are chemical substances susceptible of filtration, precipitation, and resolution. They are usually complex, and made up of an alkaloidal material and a nitrogenous substance, which is very active. It must, however, be said, that we have no precise information as to the chemical nature of bacterial toxins. They are chemically undefined substances which at present can be recognized only by biological tests; these relating especially to their specific effects upon living organisms, including the capacity to lead to the production within the animal body of specific antitoxins.

Inasmuch as we have no multiplication of bacteria, and consequently no formation of toxins, we have an explanation for the absence of inflammation when the bacteria just mentioned are introduced into the conjunctival sac of the rabbit. But when we do get inflammation—as, for instance, when these same bacteria under certain conditions find their way into the human conjunctival sac—what part do the toxins play in causing this inflammation? This is the problem under consideration.

The question as to the part played by the toxins in inflammations of the eye is one which has not led to much discussion, still less to original research. The only experimental studies which have been made on the subject are by Bardelli,[6] Druault and Petit,[7] Henri Coppez,[8] and Morax and Elmassian.[4] The first two communications are very brief, and while suggestive, they cover too little ground to rank with the work either of Coppez or of Morax and Elmassian.

The contribution of Coppez contains an account of experiments made with a view of ascertaining more particularly the manner in which the toxins secreted in the conjunctival sac act upon the cornea. One can take as a typical disease diphtheria of the conjunctiva. He finds that the diphtheritic toxin acts upon the anterior surface of the cornea. The epithelium offers a certain resistance to the action of the toxin, but when the former breaks down the cornea undergoes rapid changes. Anything now which produces a lesion of the anterior surface of the cornea would aggravate the trouble. For example, the epithelium can be injured by the very act of making applications to the eye in the course of the treatment; the constant brushing of the cornea by the false membrane on the upper lid can easily produce a disturbance in the corneal epithelium; and, finally, the action of the toxin itself upon the epithelium, which is often macerated after about forty-eight hours.

Contrary to the results of Gosetti and Iona,[9] the experiments of Coppez demonstrate that the tears have no antiseptic influence upon the diphtheria bacillus. The toxin of diphtheria has a real action upon the cornea.

The streptococcus toxin has very little action upon the cornea, and Coppez has shown that many of the phenomena observed by Bardelli in his experiments were due not to the toxins, but either to the bouillon or to the dead bodies of the microbes, or possibly to the substances which were added to the bouillon in order to kill the microbes. The pneumococcus toxin has also very little effect upon the cornea; and this is due not only, as Druault and Petit believe, to the peculiar or special resistance which the corneal epithelium offers to this toxin, but, above all, to the feebleness of the latter.

The toxins of the staphylococci, the effects of which have also been studied by Soloview and Molodorosky,[10] reproduce on a small scale pretty much the same lesions as the staphylococci themselves.

The most valuable study, however, up to 1899, was made by Morax and Elmassian,[4] and the results of their experiments were embodied in a communication made to the Ninth International Ophthalmological Congress at Utrecht, in August, 1899. These observers instilled into the rabbit's conjunctival sac the toxins of the gonococcus, of the Koch-Weeks bacillus, of the Morax-Axenfeld diplobacillus, and of the staphylococcus. Their work is far more comprehensive than any previous communication upon the subject. They were able to produce in rabbits a conjunctivitis by instilling into the conjunctival sac either a suspension of the dead organisms or the filtrate of these cultures. Of course, these organisms do not multiply in the conjunctival sac of the rabbit; and it is for this reason, as has been stated, that we only get negative results when we try to produce a conjunctivitis in this animal

by inoculating with exudates or infectious material taken from the human conjunctiva.

As regards the toxins of the organisms just mentioned, the experiments of Morax and Elmassian show that the ocular mucous membrane of the rabbit reacts under the influence of these toxins very much as does the human conjunctiva. These toxins do not seem to have much penetrating power, as prolonged contact is necessary in order to get the characteristic reaction. The reaction is not immediate, for there is always an interval of two or three hours between the commencement of the instillation and the moment of the appearance of the reactional symptoms. The different toxins do not seem to be characterized by the same kind of reactional symptoms. The reaction following the instillation of the gonococcus toxin was a little more persistent than that of either the Koch-Weeks bacillus or of the diplobacillus, while the toxins of none of these organisms produced so intense a reaction as the diphtheria toxin. These observers made thirty-eight experiments.

In October, 1899, a few weeks before I had seen either the work of Coppez or of Morax and Elmassian, I had commenced an experimental study along these lines. In a work of this character one would naturally select the toxins of those organisms which were known to be concerned in the production of certain ocular inflammations, as, for instance, the gonococcus, the diphtheria bacillus, and the pneumococcus. In addition to these organisms I experimented with the toxins of the staphylococcus aureus, micrococcus epidermidis albus, streptococcus pyogenes, bacillus coli communis, and bacillus xerosis, each of which, with the exception of the micrococcus epidermidis albus, has been placed on record at various times as being more or less concerned in producing inflammation of the eye in some form or other. For example, the staphylococcus aureus is related to a number of inflammatory conditions of the cornea and conjunctiva, being found on the margins of the lids in blepharitis and phlyctenular conjunctivitis. This organism is often found in blennorrhœa of the lacrymal sac, and in mixed infections in most corneal ulcers except in the so-called "pneumococcus ulcer" (serpent ulcer).

The micrococcus epidermidis albus is a less pathogenic organism than the preceding one; and while I can find no record which would indicate that it was the principal agent in an inflammation of the eye, I am of the opinion that under suitable conditions it is pathogenic, and that in many of our more common conjunctival and corneal troubles, to say nothing of post-operative inflammations, this organism plays a part.

The streptococcus pyogenes is sometimes the cause of corneal ulcer, and it is also concerned in various suppurative processes in the eye. This organism is not infrequently present in purulent dacryocystitis,

either alone or mixed with other bacteria, and there is a form of membranous conjunctivitis generally seen in children, and which is caused by the streptococcus, and known as streptococcus diphtheria of the conjunctiva.

The bacillus coli communis is on record as having caused panophthalmitis.[11] Groenouw[12] has observed this organism in catarrhal conjunctivitis of the newborn.

The xerosis bacillus, like the micrococcus epidermidis albus, is often found in the normal conjunctival sac, and, like the latter organism, probably plays a part in many of the inflammations in this locality.

The toxins were obtained by filtration, though sometimes the dead cultures were used.

I have divided this work into four parts: Part I. The effect produced by toxins when they are instilled into the conjunctival sac. Part II. The effect produced by toxins when they are injected into the conjunctiva. Part III. The effect produced by toxins when they are injected into the anterior chamber. Part IV. The bacteriology of the normal conjunctiva of the rabbit, based upon an examination of forty-seven cases.

Part I. The Effect Produced by Toxins when they are Instilled into the Conjunctival Sac.

Technique. The filtrate was obtained as follows: An inoculation was made from a pure culture of the organism into an Erlenmeyer flask which contained bouillon free of sugar. It is necessary for the bouillon to be free of sugar, as the presence of the latter has been shown to inhibit more or less the production of toxins. The inoculated bouillon is placed in the incubator and allowed to remain there for at least two weeks.

It is well that this amount of time be allowed for the growth of the organisms, for in this way we obtain a filtrate which is much richer in the so-called products of these organisms.

Cultures and cover-slips are then made from this mixture to see whether the original organism is present in pure culture. If these two tests result satisfactorily the fluid is passed through a Pasteur filter into a sterile Erlenmeyer flask. Inoculations are made from this filtrate on "slant agar," and both the tube and the filtrate are placed in the incubator. If at the end of three days there is no growth in the agar, and the filtrate has remained perfectly clear, the evidence is sufficiently conclusive that the filtrate contains no bacteria.

The animal is wrapped up tightly in a towel, which is carried up well around the neck, and in this position the rabbit can be kept absolutely quiet.

When the experiment lasted longer than two hours the animal was allowed to move about on a large table which was free of obstructions, and here the chances of infection were slight as compared to the chances of infection when in either a large cage or in the enclosure with the other animals.

A long sterilized dropper was used to instil the filtrate into the conjunctival sac, and when it was not being used it was kept in a vessel of sterile water.

In those experiments which lasted for two hours and less the conjunctival sac was kept full of the filtrate all the time. When the animal was allowed to run around on the table the instillations were made every few minutes, and in this way the experiment could be started at 8.30 in the morning, and, with the exception of the hour between 12 o'clock and 1 P.M., kept up until 5.30 in the afternoon. None of the experiments lasted longer than eight hours, and the shortest time was fifteen minutes. The animal was kept under the closest observation for two days after the experiment, and anything approaching a reaction was noted. Such, then, was the technique of the experiments performed in this division of the work.

Gonococcus Toxin. According to Christmas,[13] the gonococcus toxin is found partly in the body of the organism and partly dissolved in the culture medium. It is albuminoid in character, soluble in glycerin, precipitated by strong alcohol, and is destroyed by any considerable exposure to a high temperature. It is possible to produce immunity in animals by inoculating with increasing doses. Wassermann[14] is of the opinion that the toxin is confined to the body of the organism, and that no toxic products are found in the culture medium. He thinks that feeble traces of a toxin in the medium indicate that this toxin has diffused from the dead bodies of the bacteria. He was unable to produce immunity in animals.

Nicolaysen[15] found that the body of the gonococcus contained a toxin which in small doses would kill a mouse, but his filtered cultures appeared to be inert.

Laitinen[16] found only slight evidence of a toxin in the body of the organism. He holds that the filtered culture contains no toxic substance; at any rate, it is so feeble as not to be distinguishable in its effects from those of the culture medium.

Schaeffer[17] seems to be the only one besides Christmas who obtained toxic cultures. He found that the injection of cultures freed of the organisms into the human urethra produced an acute inflammation accompanied with a purulent discharge. He does not seem to have studied the effect of this toxin upon animals. I may add that the inflammatory reaction following the injection of the dead organisms into the urethra has been studied by Panichi[18] and by Scholtz.[19]

It will be seen from this that several investigators failed to get cultures which contained a soluble toxin. Christmas says that this is due to the fact that defective media were employed, and he has shown that slight differences in the composition of the medium and slight deviations in temperature are sufficient to render a culture atoxic.

The observations of Christmas are fully borne out by my experiments, and I am convinced of the existence of a toxin in the filtrate from a gonococcus culture. This fact is brought out very forcibly in the experiments where the filtrate was injected into the conjunctiva. (Part II.)

I stated that the dead cultures of the organisms were used in only a few instances, and in such cases the growth was always on "slant agar" (two parts plain sugar and one part hydrocele fluid). When the growth was eight days old its surface was covered with about an inch of chloroform, which was not poured off for twelve hours. Six hours later, when every trace of the chloroform in the tube had evaporated, the growth was scraped off and mixed up in a test-tube with sterile water or with sterile bouillon. When the filtrate was used the culture medium consisted of one part bouillon and two parts hydrocele fluid.

Case I.—White rabbit. Instillations of dead cultures mixed with sterile bouillon into the conjunctival sac of both eyes. This was kept up for fifteen minutes, during all of which time the conjunctival sacs were more or less full of the bouillon. *No reaction.*

Case II.—White and gray rabbit. Both eyes. Instillations lasted for one hour. *No reaction.*

Case III.—White and black rabbit. Instillations lasted for one and a half hours. *No reaction.*

Case IV.—White rabbit. Instilled filtrate of gonococcus culture into right eye continuously for two hours. *No reaction.*

Case V.—Same rabbit. Instilled filtrate into left eye for three hours. *No reaction.*

Case VI.—Gray rabbit. Here the instillations lasted for five hours, at the end of which time there was decided ocular and palpebral congestion. The instillations in this case were kept up for seven hours, and at the end of this time there was conjunctivitis and slight mucopurulent discharge. A repetition of this experiment in the other eye gave *a negative result.*

Case VII.—Gray rabbit. Instilled dead organisms suspended in sterile bouillon into right eye for eight hours. *No reaction.*

At first sight it would appear to be possible to cause a reaction with the gonococcus toxin if the instillations were sufficiently prolonged; but I was unable to repeat this result, and I am led to think that other causes must have co-operated to produce the conjunctivitis. Very probably a tear was made in the conjunctiva during the instillations. It will be observed in the experiments immediately following this one

that the instillations were kept up for the same length of time, but with negative results. (See last half of Case VII. and also Case VIII.)

Staphylococcus Aureus Toxin. It will be remembered that the statement was made that in inflammations of the eye this organism was generally found associated with other organisms, and that it occurred in such affections as phlyctenular conjunctivitis, blennorrhœa of the lacrymal sac, and in mixed infections of the cornea. I have never met with a conjunctivitis where there was reason to believe that this organism by itself caused the inflammation.

It has been shown by van de Velde,[20] Kraus,[21] von Lingelsheim,[22] and Neisser and Wechsberg[23] that a soluble toxin—the so-called staphylotoxin—is secreted by the pyogenic staphylococci, the most interesting property of this toxin being its power to dissolve red and white blood corpuscles.

Case I.—Gray rabbit. Instillations into the right eye for fifteen minutes, during which time the toxin was constantly in contact with the conjunctiva. *No reaction.*

Case II.—Black and white rabbit. Right eye. Instillations lasted for one hour, and during this time the filtrate was continuously in contact with the conjunctiva. *No reaction.*

Case III.—White and gray rabbit. Right eye. Here the instillations were kept up for two hours, and with absolutely *no reactional symptoms.*

Case IV.—Same rabbit. Left eye. Instillations kept up for five hours. *No reaction.*

Case V.—Black and white rabbit. Left eye. Instillations continued for eight hours. *No reaction.*

Case VI.—Gray rabbit. Dead organisms suspended in sterile bouillon. Instillations kept up for eight hours. *No reaction.*

It will be seen, then, from this series of experiments that the instillation of the staphylococcus filtrate into the conjunctival sac, even when the instillations are kept up for eight hours, is followed by no reaction.

Diphtheria Toxin. I need not recall the fact that the etiology of probably the gravest of conjunctival affections (diphtheritic conjunctivitis) is bound up in the Klebs-Löffler bacillus. The sugar-free bouillon, in which medium all of my bacteria were cultivated, is, according to Spronck and Theobald Smith, a particularly suitable medium for the production of the diphtheria toxin.

Case I.—White rabbit. Right eye. The conjunctival sac was practically full of the filtrate for fifteen minutes. *No reaction.*

Case II.—Left eye of the same rabbit. The instillations were kept up for one hour, with *no reaction.*

Case III.—White and gray rabbit. Right eye. Instillations were kept up for two hours. *No reaction.*

Case IV.—Black rabbit. Right eye. The instillations were kept up for five hours. *No reaction.*

CASE V.—Same rabbit. Left eye. Instillations continued for eight hours, with *no reaction*.

CASE VI.—Gray rabbit. Right eye. Instillations of dead organisms suspended in sterile bouillon for eight hours. *No reaction*.

Streptococcus Toxin. CASE I.—Instillations for half an hour into the right eye of a white and black rabbit. During all this time the filtrate was in contact with the conjunctiva. *No reaction*.

CASE II.—Same rabbit. Instillations for two hours into the left eye. *No reaction*.

CASE III.—White rabbit. Right eye. Instillations for three hours, with absolutely *no reaction*.

CASE IV.—Same rabbit. Instillations for four hours into the left eye, with *no reaction*.

CASE V.—Gray rabbit. Right eye. Instillations for five hours. *No reaction*.

I cannot say that I was surprised at the results of the experiments in this series, for we know that subcutaneous injections of the organisms into rabbits and mice are, as a rule, without either local or general manifestations of importance. The organism is not particularly pathogenic for animals.

Bacillus Coli Communis Toxin. This is another organism which is not supposed to possess a soluble toxin, and which in this respect resembles the gonococcus and the pyogenic cocci. It may be interesting to recall a very recent communication by Victor C. Vaughan,[24] of Ann Arbor. This observer in his study of the bacterial toxins devoted a good deal of time to the bacillus coli communis. He finds that the toxin is contained within the cell, from which it does not, at least under ordinary circumstances, diffuse into the culture medium, and that it is not extracted from the cell by alcohol, by ether, or by dilute alkalies. The unbroken germs may be heated to a high temperature with water without destruction of the toxin, and the same result follows boiling with a 0.2 per cent. aqueous solution of hydrochloric acid; but when the acid is increased from 1 to 5 per cent. the cell wall is broken up and the toxicity lessened, but not destroyed.

The toxin separated from the cell wall by digestion of the latter with hydrochloric acid and pepsin is markedly active.

It will be remembered that this organism has been discovered in pure culture in a case of panophthalmitis, and that several observers report its occurrence in unusual forms of conjunctivitis.

CASE I.—Gray rabbit. Right eye. Instillations lasted for fifteen minutes, and the contact was constant. *No reaction*.

CASE II.—Same rabbit. Left eye. Instillations for one hour. *No reaction*.

CASE III.—Black and white rabbit. Instillations for two hours into the right eye, and during this time the contact of the filtrate with the conjunctiva was constant. *No reaction*.

CASE IV.—Same rabbit. Left eye. Instillations kept up five hours. *No reaction.*

CASE V.—Left eye of rabbit used in Case I. Instillations kept up for eight hours. *No reaction.*

A negative result, then, was obtained in every case in this series. Even when the instillations are kept up practically all day the conjunctiva gives no evidence of inflammation.

Pneumococcus Toxin. CASE I.—White rabbit. Right eye. Instillations kept up for fifteen minutes. *No reaction.*

CASE II.—Same rabbit. Left eye. Instillations for one hour, with *no reaction.*

CASE III.—Black rabbit. Right eye. Instillations for three hours. Absolutely *no sign of reaction.*

CASE IV.—Same rabbit. Left eye. Instillations kept up for five hours, with the *same result as in Case III.*

Micrococcus Epidermidis Albus Toxin. This organism has been found by a number of observers in the normal conjunctiva, and by Randolph[1] eighty-eight times out of a hundred individuals whose conjunctivæ were examined.

CASE I.—White rabbit. Right eye. Instillations for one hour, during which time the contact was constant. *No reaction.*

CASE II.—Same rabbit. Left eye. Instillations for two hours. *No reaction.*

CASE III.—Black and white rabbit. Instillations into both eyes for three hours. *No reaction.*

CASE IV.—Same rabbit. Instillations into right eye for seven hours. *No reaction.*

As might have been expected from the results obtained in the preceding series, I was unable to get a conjunctivitis by prolonged instillations with the filtrate of this organism.

Xerosis Bacillus Toxin. This organism, which morphologically is so much like the diphtheria bacillus, is frequently found in the normal conjunctiva, and, like the white skin coccus, is no doubt concerned in many of the more common external eye inflammations.

CASE I.—Right eye. Instillations for one hour, during which time the filtrate was in constant contact with the conjunctiva. *No reaction.*

CASE II.—Same rabbit. Left eye. Instillations for two hours. *No reaction.*

CASE III.—White and gray rabbit. Instillations for four hours into right eye. *No reaction.*

CASE IV.—Same rabbit. Left eye. Instillations for five hours. *No reaction.*

It will be seen that forty experiments were performed in this part of the work. In many instances the filtrate was kept in constant contact with the conjunctiva for hours, and only once did I succeed in exciting

a conjunctivitis (Case I., p. 783); and I think the interpretation which I gave of this case is probably the proper one—an interpretation which is strengthened by the uniformly negative results obtained in the other thirty-nine cases.

With the exception, then, of this case, the results of the instillations of the filtrates into the conjunctival sac are directly opposed to the results which were obtained by Morax and Elmassian.

Part II. The Effect Produced by Toxins when they are Injected into the Conjunctiva.

There is probably no part of the body which is as able to fight with infectious bacteria as the eye. When we consider how frequently the eyeball is wounded not only by accidents, but also by operative measures, and how comparatively seldom pathogenic infection results, we are forced to the conclusion that the eye must enjoy immunity to a high degree. This immunity or resistance to disease is partly accounted for, no doubt, by the exceptional activity of the leucocytes of the eye. This activity is remarkable in the case of the rabbit's eye, in which animal a considerable wound of the cornea will in twenty-four or forty-eight hours have vanished and left hardly a trace.

In our daily practice we often see the same thing to a less marked degree, and it suggests that the strength of the eye lies not only in the peculiar activity of its leucocytes, but also in the properties of its fluids, which are probably to some extent antibacterial. I need not bring forward evidence to show how much happier have been the issues from operations upon the eye since the advent of Listerism and of all that this word means. That goes without saying, but I think I am quite safe in saying that Listerism found no part of the body so well equipped to take care of its bacteria as the eye. While the mortality (if I may use the word) is less nowadays, the difference in this respect is much less startling than it is in the other fields of surgery.

It is perfectly clear from a study of the foregoing experiments that the rabbit's eye is quite able to withstand the harmful effects of the instillation of toxins upon its surface, no matter if these instillations are kept up practically all day. The question is, can this immunity of the eye nullify the effects of these toxins when they are injected into or have gained a foothold in the tissues?

Technique. The syringe and fixation forceps were boiled five minutes. The eye of the rabbit was anæsthetized with holocaine. The animal was always wrapped in a towel, as in the first series of experiments, in order to keep it immovable. The operation was apparently painless.

In the first place, the conjunctivæ of five eyes were injected with sterile bouillon, to see whether any reaction could be produced by the

medium. Varying quantities were injected, up to as much as a syringeful.

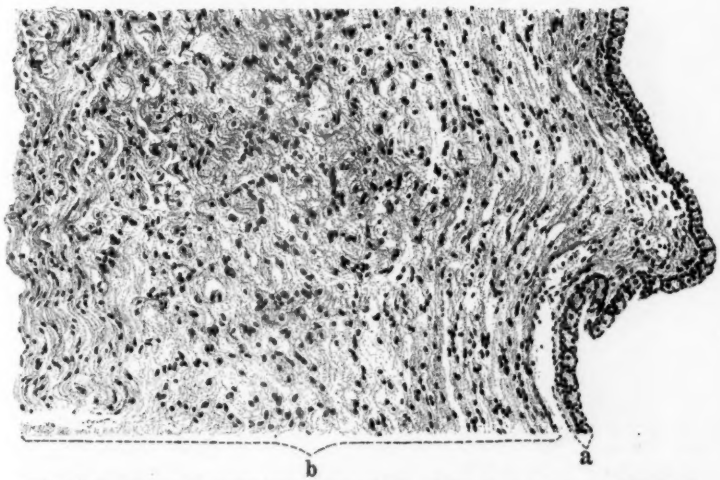
With the exception of one case in which there was some difficulty in penetrating the conjunctiva, and where there was, in consequence, bruising of the latter, there was no reaction. In the case mentioned it was noticed that the syringe leaked. It was withdrawn, and on inserting it again the conjunctiva was torn.

I always endeavored to make the injection at one point in the conjunctiva, which at this location at once puffed up and looked like a big blister.

The operations were performed in the afternoon, and the eyes were examined the next day at the same time.

There was no particular point selected for the injection, though usually it was made above the cornea, at about half an inch from the margin of the latter.

FIG. 1.



Section from the normal conjunctiva of the rabbit. (Zeiss, oc. 4; obj. a a. Enlarged 90 times.) *a*. Epithelial layer. *b*. Connective-tissue layer.

Gonococcus Toxin. CASE I.—Gray rabbit. Injected ten drops of filtrate into the conjunctiva of the right eye, and into the conjunctiva of the left eye the same quantity of sterile bouillon. The next day there was intense reaction in the right eye and no reaction in the other eye.

CASE II.—Gray rabbit. Right eye. Injected eight drops into the conjunctiva. The next day there was marked congestion of the upper half of the eyeball, much more intense at the point of penetration.

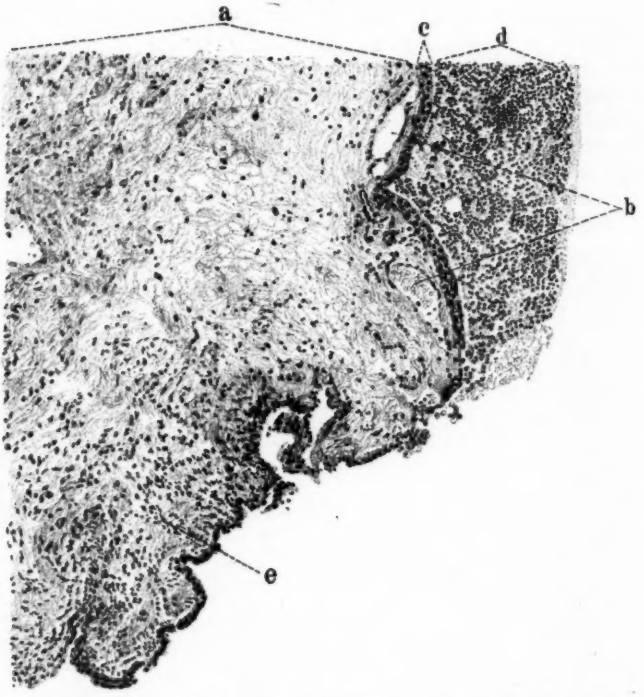
CASE III.—White and black rabbit. Right eye. Injected five drops

of the filtrate. Conjunctivitis possibly not so marked as in either of the last cases.

CASE IV.—Same rabbit. Injected three drops of the filtrate. The next day a slight redness near point of injection, covering about a fourth of the globe.

Diphtheria Toxin. CASE I.—White rabbit. Injected ten drops of filtrate into the conjunctiva of the right eye and ten drops of sterile bouillon into the left. At the end of twenty-four hours there was

FIG. 2.



Conjunctivitis. Gonococcus toxin. Case I. (Zeiss, oc. 4; obj. aa. Enlarged 90 times.) *a*. Connective-tissue layer. *b*. Distended bloodvessels. *c*. Epithelial layer. *d*. Large exudate resting upon the epithelial layer. *e*. Area in connective-tissue layer crammed with leucocytes and round cells.

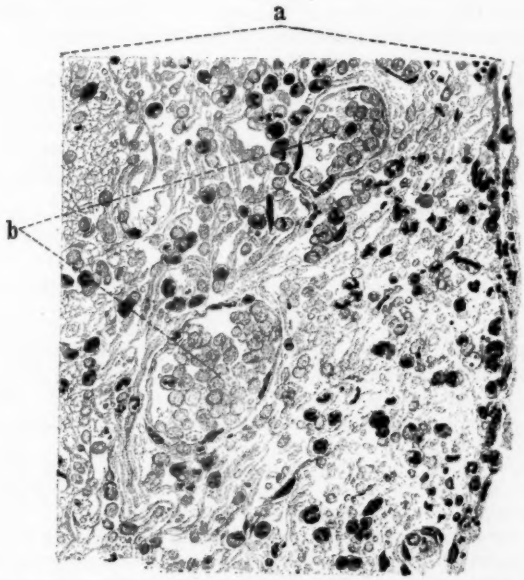
intense reaction in the right eye. There was an almost typical picture of diphtheritic conjunctivitis. The swelling of the lids was so great that the animal could not open its eye. When the lids were forcibly opened there was a welling up of a purulent discharge, and there was a strong suggestion of a membrane on the upper lid. The cornea was rather dull. The left eye, into which ten drops of sterile bouillon had been injected, showed no reaction. This was the only case in which I obtained a reaction which resembled the picture seen in the human being.

The same filtrate was used for an instillation experiment and the instillations kept up nearly all day, but with negative result.

Welch and Flexner have shown that the poison producing the false membrane is an intracellular one, and not the soluble toxin, so that a definite pseudomembrane is not to be expected after injecting the latter alone.

CASE II.—White rabbit. Right eye. Injected eight drops of the filtrate. The next day there was marked conjunctivitis, with possibly a little excess of secretion.

FIG. 3.



Conjunctivitis. Intense hemorrhagic inflammation. Diphtheria toxin. Case I. (Zeiss, obj. D D; oc. 4; enlarged 420 times.) *a*. Connective-tissue layer which is very œdematous. Red blood corpuscles and polynuclear leucocytes may be seen everywhere throughout this section. *b*. Engorged bloodvessels.

CASE III.—Same rabbit. One week later. Injected into left eye six drops of filtrate. Twenty-four hours later there was conjunctivitis which did not differ materially from the condition which was seen in Case II.

CASE IV.—White and black rabbit. Left eye. Injected three drops of filtrate. The next day there was conjunctivitis which consisted in simple congestion of the upper half of the eyeball, with no discharge.

Pneumococcus Toxin. CASE I.—White rabbit. Injected fifteen drops of filtrate into the conjunctiva of the right eye and the same quantity of sterile bouillon into the conjunctiva of the left eye. The next day the

right eye showed marked conjunctivitis which extended over the entire eyeball, while the result of the injection in the left eye was negative.

CASE II.—Injected left eye of the same rabbit. Eight drops of filtrate were used. Twenty-four hours later conjunctivitis, with no increased secretion.

CASE III.—White and black rabbit. Injected six drops of filtrate into the conjunctiva. The next day there was conjunctivitis which did not differ materially from the condition in the preceding case.

CASE IV.—Same rabbit. Left eye. Injected three drops of filtrate. The next day there was redness of the conjunctiva near the point of the injection, but the inflammation in this case was very localized.

Streptococcus Toxin. CASE I.—Injected fifteen drops of filtrate into the conjunctiva of the right eye and the same quantity of sterile bouillon into the conjunctiva of the left eye. Next day pronounced conjunctivitis, which was uniformly distributed. The left eye showed no change.

CASE II.—Same rabbit. Few days later. Injected ten drops of filtrate into left eye. Conjunctivitis the next day. Possibly somewhat less marked than in the preceding case.

CASE III.—White rabbit. Injected ten drops of filtrate into right eye. The next day conjunctivitis, which was pretty uniformly distributed.

CASE IV.—Same rabbit. Left eye. Injected eight drops of filtrate. Next day there was conjunctivitis which differed very little from the reaction seen in Case III.

CASE V.—White and black rabbit. Right eye. Injected five drops of filtrate. Next day there was slight conjunctivitis.

Staphylococcus Aureus Toxin. CASE I.—White rabbit. Injected into the right eye fifteen drops of filtrate. The next day there was marked conjunctivitis which differed in no respect from the conjunctivitis which was seen in Case I. in the preceding series. The other eye, into which the same quantity of sterile bouillon was injected, showed no reaction.

CASE II.—White and gray rabbit. Injected ten drops of filtrate into right eye and the same quantity of sterile bouillon into the left eye. The next day the right eye showed conjunctivitis. There was also some congestion of the left eye, but I am disposed to attribute the reaction in this eye either to bruising of the tissues or to some accidental infection which occurred after the experiment.

CASE III.—Same rabbit. One week later. Injected eight drops of filtrate into left eye. The next day there was conjunctivitis, but not nearly so marked as in Case I.

CASE IV.—White and black rabbit. Right eye. Injected five drops into the conjunctiva of this eye and five drops of sterile bouillon into the conjunctiva of the left eye. Slight conjunctivitis in the right eye and no reaction in the left eye.

Bacillus Coli Communis Toxin. CASE I.—Black rabbit. Injected fifteen drops of filtrate into the right eye and the same quantity of sterile bouillon in the left. The next day there was almost as intense a reaction in the right eye as was seen when ten drops of the gonococcus and diphtheria toxins were used. The left eye showed no reaction.

CASE II.—Same rabbit. Left eye. Injected ten drops into the conjunctiva. The next day there was quite a marked conjunctivitis.

CASE III.—White and black rabbit. Right eye. Injected eight drops of filtrate. The next day there was conjunctivitis not differing materially from what was seen in the preceding case.

CASE IV.—White rabbit. Injected three drops into the conjunctiva of left eye. The next day there was slight congestion in the upper half of the eyeball, more marked near the point of the injection.

Xerosis Bacillus Toxin. CASE I.—White rabbit. Injected fifteen drops of filtrate into the right eye and fifteen drops of sterile bouillon into the left. The next day there was marked conjunctivitis in the right eye and no reaction in the left eye.

CASE II.—Same rabbit. Left eye, a few days later. Ten drops of filtrate injected. Conjunctivitis, but less marked than in the preceding case.

CASE III.—White rabbit. Injected into the right eye five drops of filtrate. Next day there was conjunctivitis not differing materially from Case II.

Micrococcus Epidermidis Albus Toxin. Three experiments were performed in this series, and they resulted practically as did those in which the xerosis bacillus was employed.

It will be seen that thirty-one experiments were performed in this series, with a positive result in every case—a marked contrast to the results which were obtained in Part I.

I have more than once recalled the fact that several of the organisms with which I have experimented are not supposed to produce soluble toxins. The uniformly positive results which were obtained in Part II. suggested that possibly the effect produced was due to the presence in the filtrate of some of the so-called bacterio-proteins described by Buchner, and which are distinctly irritating. These products are incorporated in the substance of the bacterial cells, and are set free especially from degenerated or dead bacteria. The older a culture the greater the number of dead or degenerated bacteria which it contains. It is evident, then, that these bacterio-proteins are more abundant in a culture say of two weeks' growth than in one which is only twenty-four hours old. It will be remembered that my cultures were usually allowed to remain undisturbed for two weeks, as in this time I obtained a more concentrated culture, and consequently a more satisfactory filtrate.

To eliminate to a considerable extent the agency of these bacterio-proteins the cultures were filtered when they were only twenty-four hours old. Five experiments were made with a filtrate of this character.

CASE I.—White rabbit. Ten drops of filtrate were injected into the conjunctiva of the right eye. Same quantity of sterile bouillon was injected into the conjunctiva of the left eye. The next day there was a well-marked redness of the right eyeball, while the left eye showed no change. The toxin in this case was of *staphylococcus pyogenes aureus.*

CASE II.—*Same Toxin.* Same rabbit. Left eye. Ten drops of filtrate were injected. The result was the same as in Case I.

Bacillus Coli Communis. CASE I.—White and gray rabbit. Right eye. Injected ten drops of filtrate into the conjunctiva. A decided conjunctivitis followed.

CASE II.—Same rabbit. Left eye. Ten drops of filtrate were injected into the conjunctiva. Next day there was a slight conjunctivitis.

Diphtheria Toxin. CASE I.—Black rabbit. Right eye. Injected ten drops of filtrate into the conjunctiva and the same quantity of sterile bouillon into the conjunctiva of the other eye. There was a conjunctivitis in the right eye the next day and slight redness of the fellow eye, which latter condition I interpreted as being due, in all probability, to some mechanical injury of the conjunctiva at the injection.

It will be seen from this that the elimination to a large extent from the filtrate of the bacterio-proteins had scarcely more than an appreciable effect upon the character of the reaction. In these last five cases the congestion of the conjunctiva was possibly a little more localized around the point of the injection than was the case in the other experiments of this division of the work, and this we might interpret as being due in part to the feebler concentration of the culture as well as to the smaller quantity of bacterio-proteins.

PART III. THE EFFECT OF THE TOXINS WHEN THEY ARE INJECTED INTO THE ANTERIOR CHAMBER.

The following was made as a control experiment: A Graefe cataract knife was passed into the cornea at its upper scleral border. Through this incision ten drops of sterile bouillon were injected into the anterior chamber. The next day, with the exception of a very small hernia of the iris and three or four vessels grouped at the point of the wound, the eye was normal. On the second day the congestion had entirely disappeared, but the slight irregularity in the pupil persisted, and this is due to the incarceration of the iris in the lips of the incision, and it will never disappear. There was, however, not the slightest sign of an iritis.

The following experiments were then made:

Gonococcus Toxin. CASE I.—White rabbit. Right eye. Anterior chamber was opened as in the preceding case and five drops of the filtrate injected from a hypodermic syringe. The next day there was pericorneal congestion, which was more marked at the point of the incision. The aqueous was slightly cloudy. Iritis. In seven days the symptoms had entirely disappeared.

Diphtheria Toxin. CASE II.—Same rabbit, ten days later. Left eye was utilized. An incision was made in the usual manner above, just as we do in a cataract incision, except that the incision in the experiment is, of course, much smaller. Ten drops of the filtrate were injected through this incision into the anterior chamber. The next day there was a very intense iritis, showing itself in practically the same symptoms as in Case I. The eye had cleared up in a week.

Bacillus Coli Communis Toxin. CASE III.—Gray rabbit. Injected ten drops of filtrate into the anterior chamber above. Next day there was iritis, with the usual symptoms.

Pneumococcus Toxin. CASE IV.—Gray rabbit. Left eye. Injected into the anterior chamber ten drops of the filtrate. In twenty-four hours there was iritis, which did not differ materially from what was seen in Case II.

Staphylococcus Aureus Toxin. CASE V.—White and black rabbit. Right eye. Ten drops of filtrate were injected into the anterior chamber. Result was the same as in the last two cases.

Micrococcus Epidermidis Albus Toxin. CASE VI.—Ten days later fifteen drops of the filtrate were injected into the anterior chamber of the left eye. I saw no material difference in the reaction from that in the preceding case.

At first sight one would suppose that the reaction in experiments of this character would be more intense, more destructive than when the injection was made into the conjunctiva. The absence of panophthalmitis and closed pupil is explained by the fact that some at least of the filtrate oozed out of the anterior chamber. As long as the wound was open, and no doubt it remained so for several hours, there was more or less oozing. The filtrate which remained was certainly considerably diluted by the rapidly regenerating aqueous, so the toxin in its original condition remained for a very brief space of time in the anterior chamber, but quite long enough to light up inflammation; and no doubt is left in my mind that had I injected the toxin through a needle-hole opening right into the anterior chamber serious results would have followed, for in this case the tension of the eye would have been markedly increased, and the toxin would have been retained.

In the conjunctival injections the needle-hole closed on withdrawing the needle, and there was apparently no oozing, the bleb remaining for some little time after the experiment.

We have evidence enough to show, then, that the filtrate from the cultures of the organisms which were used in these experiments is sufficiently irritating to set up inflammation in the conjunctiva and in the iris. That the bacteria in the rabbit's conjunctiva play a part in this inflammation is almost certain. The effect of the toxin is simply to irritate, and in this way to lessen local resistance. We know that the normal human conjunctiva is rarely if ever free of bacteria, several of which have very slight pathogenic properties, but that when an irritant is applied to the eyeball the conditions are at once produced under which these very organisms become pathogenic and do harm

Mention has been made of several works upon the bacteriology of the normal human conjunctiva; but, so far as I know, no work has been done upon the bacteriology of the rabbit's conjunctiva—an important omission when we consider that practically all of the experimental work of the ophthalmologist is done upon the rabbit's eye.

It has occurred to me, in this connection, to make an examination of the normal conjunctiva of the rabbit, to see whether its bacteriology resembles that of the human conjunctiva, and this brings me to Part IV.

Part IV. The Bacteriology of the Normal Conjunctiva of the Rabbit Based upon an Examination of Forty-seven Cases.

The technique consisted in rubbing a rather large, sterile platinum loop over the conjunctiva of the eyeball, and carrying it well into the conjunctival sac, from which points inoculations were made into the fluid agar. Plate cultures were always made.

1. Two whitish, well-defined colonies; both micrococci.
2. Two colonies; one evidently an impurity, the other a micrococcus.
3. One colony; micrococcus, which was like the coccus found in 1 and 2.
4. One colony; similar to 3.
5. Several small colonies; whitish; all proved to be micrococci.
6. Coccus similar to preceding; a large bacillus.
7. Plate was covered with small colonies; micrococcus like 1 and 2.
8. Several colonies. The large colored ones proved to be a big bacillus. There was a streptococcus colony; also a micrococcus similar to 1 and 2.
9. Four colonies, all of which were micrococci.
10. Two colonies; one proved to be a bacillus, the other a micrococcus.
11. Micrococcus, like the preceding; also a large, yellowish colony, proving to be a big bacillus.
12. A colony which covered a large area, proving to be a big bacillus; also a micrococcus.
13. Several yellowish colonies; bacilli of different sizes.
14. Several yellowish colonies, which proved to be a short bacillus; also a number of whitish colonies, which were micrococci like 1 and 2.
15. A number of colonies; all micrococci like those seen in 14.
16. Abundant growth; micrococci like the preceding.
17. Abundant growth; micrococci like the preceding.
18. Several colonies; micrococci like the preceding.
19. Two colonies, one of which was a large bacillus and the other a large coccus.
20. One large colony, which proved to be a large coccus, and several smaller colonies, which proved to be micrococci like those frequently seen in preceding cases.
21. Several colonies; micrococcus.
22. Several colonies; micrococcus.

23. One colony; micrococcus.

24. One large colony, which proved to be a big, short bacillus.

25. Several colonies; micrococci like those in 1 and 2.

26. Several colonies; micrococci like preceding. There was a yellowish colony in this plate, but an examination of the organism showed it to be a micrococcus not differing morphologically from the other coccus.

27. Two colonies, one whitish and the other yellowish-white; micrococci which did not differ morphologically.

28. Nothing grew in this plate.

29. One large colony, covering half the plate, which proved to be the bacillus subtilis. There were other small colonies in this plate, some of which were micrococci like 1 and 2, and others were very small bacilli.

30. Three colonies, which proved to be very fine bacilli.

31. Several colonies. One was a large coccus and the others were short bacilli.

32. A number of colonies which were sharply round and white, some consisting of a large coccus, and others were micrococci.

33. Several colonies, consisting, for the most part, of diplococci and large cocci.

34. Two colonies; both diplococci.

35. Several colonies; micrococcus like that in 1 and 2; fine streptococcus.

36. Micrococcus similar to 1 and 2.

37. A number of colonies, consisting for the most part of micrococci like those in 1 and 2; also a fine streptococcus.

38. A number of colonies; micrococci like 1 and 2.

39. Rather large coccus. A number of other colonies, which were micrococci like 1 and 2.

40. Two colonies. One was a large coccus, while the other was a micrococcus like 1 and 2.

41. A number of colonies, most of which were micrococci like 1 and 2. There was also a growth which proved to be a fine streptococcus.

42. Large number of colonies which proved to be a big coccus, and one colony which was a fine streptococcus.

43. One colony; micrococcus like 1 and 2.

44. Several colonies; large coccus; micrococcus like 1 and 2.

45. Number of colonies; same micrococcus as in 1 and 2.

46. Number of colonies; same micrococcus as in 1 and 2.

47. Number of colonies; same micrococcus as in 1 and 2.

From a study of these cases it appears that the normal conjunctiva of the rabbit contains quite a variety of bacteria. There was more often found, however, a micrococcus which proved to be the staphylococcus

albus. This organism occurred in thirty-six out of the forty-seven cases (1, 2, 3, 4, 5, 6, 7, 8, 9, 12, 14, 15, 16, 17, 18, 20, 21, 22, 23, 25, 26, 27, 29, 32, 35, 36, 37, 38, 39, 40, 41, 43, 44, 45, 46, 47).

The staphylococcus albus, as we know, is feebly pathogenic; but given sufficient irritation it can and often does produce inflammation, and it is reasonable to presume that this organism was frequently concerned in causing the conjunctivitis and iritis recorded in Parts II. and III.

At any rate, the normal conjunctiva of the rabbit, like the normal human conjunctiva, is probably never sterile. In only one case (Case XXVIII.) was there a sterile plate.

Epicritical Observations. The foregoing experiments are of interest in several respects. The forty experiments recorded in Part I. indicate that simple contact of bacterial toxins with the normal conjunctiva produces no local inflammation or other injury to the animal. This is in accordance with what is already known concerning the behavior of this class of poisons when applied to other intact mucous surfaces. Unlike alkaloidal and many other kinds of poisons, the chemically undefined toxins produced by bacterial cells, as well as similar toxins produced by certain cells of higher plants (ricin, abrin) and of animals (snake venom), are in general incapable of absorption from intact mucous surfaces, although before the present series of experiments this had not been satisfactorily demonstrated in the case of the conjunctival mucous membrane.

Not only are the toxins not absorbed under these circumstances, but they do no damage to the intact epithelium. In fact, it is probably this absence of local injury induced by the bacterial toxins which explains the lack of absorption of the toxins. That there are special epithelio-toxins capable of damaging epithelial cells has been demonstrated by von Dungern[25] and others, but such specific toxins for epithelium have not been discovered in filtrates of bacterial cultures. We know, however, that certain bacterial toxins, notably the diphtheria toxin, may act injuriously upon previously altered epithelial cells, and further investigations may show the existence of bacterial toxins capable of directly injuring intact epithelium.

The experiments recorded in this paper, therefore, indicate the great importance of integrity of the epithelial surfaces in protecting against local and general injuries from toxins secreted by bacteria. We were already familiar with this protective influence in guarding against local and general infections by the bacteria themselves, although there are bacteria which can attack the normal epithelium. Inasmuch as bacteria in general are more virulent when they are accompanied by their toxins at the time of their invading the animal body, it seemed important to determine, as has been done in this paper, the action of

the toxins separated from the bacteria upon the intact conjunctival membrane.

To what extent the protection afforded by intact epithelium against bacterial toxins is purely mechanical, or is due to incapacity of the toxin to enter into a chemical union with the epithelial cell in the sense of Ehrlich's "side-chain" theory or to other causes, I have not attempted to determine. When, however, the toxin has gained access to the subepithelial tissues we find the conditions entirely different.

The numerous experiments recorded in Part II. demonstrate that filtrates from both young and old cultures of all the various bacterial species used contain some irritative poison capable of setting up local inflammation when these filtrates are injected into the substance of the conjunctival mucous membrane. Certain of the bacterial species employed produced more powerful irritative poisons than others, the strongest of these toxins being found, in the present experiments, in cultures of the gonococcus, the diphtheria bacillus, and the colon bacillus, but notable effects were obtained with cultures of the pyogenic micrococci.

That the substances concerned in producing these local inflammations are specific products of the bacteria, and are not attributable to ingredients of the original culture media, was abundantly demonstrated by the fact that control injections of the uninoculated culture media even in much larger doses were entirely without any injurious effect.

It is possible that bacteria normally present in the rabbit's conjunctival sac may have participated in causing the inflammations which regularly followed the injections of the toxins into the conjunctival membrane. In Part IV., I have shown that the normal conjunctival sac of the rabbit contains a variety of bacteria, and that among these a white staphylococcus resembling if not identical with the staphylococcus albus (staphylococcus epidermidis albus) is common. But the primary and essential damage is that which is inflicted by the toxin, as the control experiments show; and if bacteria were secondarily active it is because the soil was prepared for them by the damage done to the cells and tissues by the toxins.

I can readily understand that such ordinarily harmless bacteria as the white staphylococcus or other common bacterial inhabitants of the conjunctival sac may gain a foothold and multiply in tissues whose vital resistance has been impaired by the previous action of toxins.

After it had been determined that bacterial toxins introduced into the connective tissue of the conjunctiva cause inflammation it was not surprising to find that a similar result followed the injection of the same toxins into the anterior chamber of the eye, as is demonstrated by the experiments recorded in Part III.

There is another aspect of the experiments which is of considerable interest. Filtrates were used from cultures not only of bacteria known to produce powerful soluble toxins, but also of those not before positively known to secrete soluble toxins. Inasmuch as we have at present no means of determining whether a given bacterium secretes a toxin or not, except by the biological test, it has been generally assumed that when this test fails there is no evidence of the existence of such a toxin. But it may be asked whether in all instances sufficiently delicate tests have been made?

The need of caution in drawing conclusions in this matter is made evident by the interesting experiments of Kraus,[26] who has shown that specific soluble bacterial products previously unsuspected are present in the fluid cultures of the typhoid bacillus, the cholera bacillus, and other bacteria, and can be revealed by the action of the homologous antiserum. That toxins may have peculiar specific effects upon certain cells, and that these effects may be of such a nature that they are readily overlooked until careful search is made for them, has been shown by the discovery in recent years of the various cytolysins produced by the pyogenic staphylococci and the tetanus bacillus.

It is from this point of view of interest that all of the bacteria which I employed were demonstrated to produce toxins capable of causing injury and inflammation of the tissues of the conjunctiva. Injection into the eye, particularly into the substance of the conjunctiva, would seem, therefore, to make a more delicate biological test for the recognition of certain toxins than the tests which have usually been employed to determine this point. That the toxins concerned were not simply the so-called bacterio-proteins of Buchner, derived from degenerated and macerated bacterial cells, was proven by the determination of the toxicity of young cultures.

The experiments recorded in this paper are in harmony with clinical experience, and they shed some light upon questions of clinical interest. We know that in a large proportion of cases of infectious inflammations of the eye a lesion of continuity is demonstrable or can reasonably be inferred. This lesion is now shown to be important not only in opening a path for the invasion of bacteria and in weakening the local vital resistance to bacteria, but also in permitting the entrance of toxins which constitute the weapons by which the bacterial cells do injury. Without this opportunity for the penetration and action of toxins even highly virulent bacteria may be harmless, as has been shown in the case of the tetanus bacillus, and with this opportunity bacteria of even very weak virulence, such as the common white staphylococcus, may be pathogenic. In support of these views I need not dwell upon conditions where the injury is manifest, as in postoperative inflammations, penetrating wounds of the eyeball, serpent ulcer, etc. I am of the

opinion that many cases of gonorrhœal ophthalmia and of "pink eye" are produced not by the simple introduction of the specific bacterium into the healthy conjunctival sac, but by the bacterium acting upon a conjunctiva slightly injured, even if the injury be no more than the slight abrasion of the conjunctival epithelium which may result from rubbing the eyes with the fingers. I have seen in the last two years two cases of gonorrhœal ophthalmia resulting from the spurting of fluid from a pyosalpinx into the eye of the operator, and in each instance this accident was followed by violent rubbing of the eye, which would produce a lesion of the conjunctival epithelium.

How often we meet with gonorrhœal ophthalmia as a monolateral affection!—in fact, in the majority of cases. What a very common disease is gonorrhœa, and how comparatively infrequent is gonorrhœal ophthalmia!

It can hardly be otherwise than that the gonorrhœal virus often gains access to the conjunctival sac without setting up inflammation.

It must often happen in cases of highly infectious inflammations of one eye that the infectious germs are conveyed to the other eye without resulting injury. While every precaution should be taken to guard against such a contingency, it is probable that our protective measures are effective in many instances as much by preventing slight local abrasions as by the exclusion of the infectious bacteria.

We know that it is scarcely within the power of the surgeon to exclude absolutely all bacteria from wounds, and that in so-called aseptic wounds bacteria, sometimes even pathogenic forms, are present. Nothing is easier than the entrance of bacteria into the conjunctival sac, nor can we rid the sac entirely of micro-organisms. Whether or not bacteria there present do harm depends upon a number of circumstances, and among the most important of these circumstances is the condition as regards integrity of the conjunctival surface.

My experiments have demonstrated, I think, the importance of this factor in relation to toxins; and also that pathogenic bacteria, even those for which toxins had not previously been satisfactorily demonstrated, do harm through the action of specific soluble poisons.

What, then, is the conclusion of the whole matter?

1. Bacterial toxins, so far as tested, when instilled even for many hours into the healthy conjunctival sac were found incapable of producing inflammation or causing other injury.

2. The same toxins when injected into the tissue of the conjunctiva or into the anterior chamber invariably set up local inflammation, the extent and intensity of the inflammation varying to some degree, according to the species of bacterium yielding the toxin.

3. Bacteria which had not previously been proven to produce soluble toxins were found to produce them even in young cultures, and it is

suggested that injections of bacterial filtrates into the eye, particularly into the conjunctival tissue, constitute a more delicate biological test for the detection of certain toxins than the tests usually employed for this purpose.

4. The experiments recorded in this paper furnish additional examples, in a comparatively new field, of the importance of toxins in explaining the pathogenic action of bacteria, and likewise emphasize the etiological significance of injuries of the covering membrane of the eye in favoring the action of toxins and of bacteria.

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OSTEITIS DEFORMANS AND HYPEROSTOSIS CRANII. A CONTRIBUTION TO THEIR PATHOLOGY, WITH A REPORT OF CASES.

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THE symptomatology and general features of osteitis deformans have been so exhaustively discussed in this country within a recent period in the monographs of Elting, Wilson, and Packard, Steele and Kirkbride, that I shall limit myself in this communication to a brief

description of two cases and to the question of its pathology. The last-named writers have not only contributed a valuable addition to our knowledge of the anatomical lesions, but also an important summary of the data furnished by sixty-six cases collected from the literature.

CASE I.—Mrs. M., aged forty-four years, was referred on November 1, 1901, to my clinic at the Boston City Hospital from the Eye Department, to which she had applied for impairment of vision, but the

FIG. 1.

CASE I. Osteitis deformans, aged 44 years, showing deformity of jaw, right forearm, kyphosis and temporal artery.

FIG. 2.

CASE I. Osteitis deformans, showing enlargement of parieto-occipital region, arterio-sclerosis, and deformity of radius, right arm.

ophthalmic records note only errors of refraction. She was referred to me for certain neuralgic pains in her head. The peculiar enlargement and deformity of the cranium and jaw were noticeable and led to a careful examination of the osseous system.

As to her previous history and the family history, they were practically negative. There were no evidences of syphilis. She had not had a pain or an ache referable to her present condition until April, 1901, when she had some dizziness (heart?), and a month later she

experienced some pain in her head. From May to October she was free from pain and all other symptoms excepting the impaired eyesight, for which she was fitted with glasses. On November 1st her symptoms were mild, and, such as they were, consisted of neuralgic

FIG. 3.

CASE I. Osteitis deformans; right radius, showing curvature.

pains in the head, tinnitus aurium and cardiac fluttering. Until two years ago she had never noticed any deformity of the bones—not until the curvature and enlargement of the right forearm were pointed out to her by a friend—and when first examined she was entirely uncon-

scious of the extreme deformity of the skull that exists and of the obtrusive bending and thickening of the bones of the legs.

On first inspection, aside from the asymmetry of the skull and jaw, the most noticeable peculiarity about her is the general degeneration of her physique. She looks much older than she is; she is short of

FIG. 4.

CASE I. Right femur. (The curvature and hypertrophy would be more apparent if the whole length of the bone were reproduced in the cut.)

stature, bent over, and has generally small, poorly developed muscles. There is a lack of color and vascularity of the skin, which has a dried and slightly yellow appearance. Physical degeneration is stamped upon her. She looks shrunken in height and development. On her temples enlarged and tortuous atheromatous arteries stand out and strike the eye. The heart is enlarged, the apex being one inch outside

the mammillary line, but in the fifth space, and its action is heaving. A systolic murmur is heard over the aortic valves and at the apex whither it is probably transmitted. The eyes are unusually prominent. (Figs. 1 and 2.)

Osseous System. The condition of the bones resembles in general that which has been frequently described in cases of osteitis deformans. The cranium is irregular and enlarged, although the hyperostosis is most obtrusive in the left parietal bone. The circumference of the fronto-occipital region is 61½ cm. The ramus of the jaw on the right is thickened and prominent to the eye; the spine is very slightly flexible, and has a marked kyphosis in the upper dorsal region. There is some deformity of the sternum from thickening; both clavicles are enlarged, the ribs thickened. The bones of the upper arms appear to be normal; but both radii, the right being the most affected, are thickened and curved, the bowing being outward. The last phalanges of the first and second fingers of both hands exhibit nodular thickenings and are distorted, being everted at an angle outward, giving the *impression of an osteo-arthritis.*

Coming to the lower half of the body, both femora are curved and greatly thickened, as are the tibiæ. As in the forearm, the right side is more largely affected than the left; the bones of the pelvis are also involved in the process. The photographs and skiagraphs show fairly well the conditions present. Examination of the blood failed to throw any light on the morbid process, showing simply a mild secondary anæmia.[1] Examination of the nervous system at this time was negative.

Since my last examination of this patient she entered the Massachusetts General Hospital, where she came under the observation of Dr. Fitz, who also has made a careful study of her condition. While in this hospital she developed delusions and other mental symptoms, and was removed to the Boston Insane Hospital, where she now is under the charge of Dr. Lane, who has kindly furnished me with notes of her present condition, which is that of a rather mild stupor, with some depressions and delusions.

The most interesting problems connected with this most interesting disease are its pathology and its relation to allied affections. The symptomatology has been adequately and exhaustively discussed within the limits of our present knowledge in the paper presented to this Association by Drs. Packard and Steele at the last meeting. It will be remembered that the basic and anatomical process in osteitis deformans as shown by the microscopic changes was summed up (but as I shall show incompletely) by these authors as follows:

"*a.* Absorption of the compact substance, causing enlargement and confluence of the Haversian canals.

"*b.* Formation of new bone, which runs diffusely through the affected and the adjacent healthy portions. This new bone remains uncalcified, and is in turn reabsorbed.

[1] White count, 3800; red count, 3,768,000; hæmoglobin, 65 per cent. Differential count: polymorphonuclear neutrophiles, 66 per cent.; small lymphocytes, 26 per cent; large lymphocytes, 6 per cent.; eosinophiles, 2 per cent.

"*c.* The conversion of the medullary substance into a vascular connective tissue containing fat cells, giant cells, and leucocytes.

"*d.* As a consequence of these three processes the ordinary relations of the compact substance and medulla are destroyed. The bones become exceedingly thickened and asymmetrical, but since the new bone tissue remains uncalcified its elasticity permits of great deformity of the long bones from the weight of the body, and fractures do not occur."

This summary is incomplete in that it neglects to take into account the important fact that often *calcification does take place in the new bone*, and then a different picture is presented.

Clinically considered, the disease resembles in the peculiar enlargement and deformity of the skull what has been noted and described in hyperostosis cranii, or leontiasis ossia, and although the two diseases are regarded as distinct, it is interesting to reconsider whether, after all, hyperostosis cranii may not be an incomplete development of the same process, and, therefore, the same disease. Putnam,[1] in his exhaustive and critical paper, in 1896, has already recorded one case of my own of hyperostosis cranii. I have now to report another interesting case, which in general appearance and certain other respects bears a most striking resemblance to the case of osteitis deformans I have just reported.

CASE II.—The patient, Miss A., is sixty-three years of age, and looks about ten years older. Her general physical appearance is that of degeneration. She is short and considerably shrunken from her former height, due to the marked kyphosis in the cervico-dorsal region. The anterior borders of the ribs correspondingly approximate the pelvis. There is very marked arterio-sclerosis, which is particularly obtrusive in the temporal arteries, which stand out prominently tortuous and rigid, as in Case I. The eyes are rather prominent and the face thin. All the muscles of the body are extremely small, simulating a dystrophy. The arms, for example, would be small for a child. There are certain nervous symptoms of an atypical character. There is no paralysis, but a decided myasthenia. The gait is shuffling and unsteady, as if rather from a lack of confidence than from any real ataxia; deep reflexes are normal. There are no sensory disturbances. Her ideation is not normal, and yet it is not easy to give it a definite characterization. There is a tendency to fads, eccentricities, and fixed ideas. For example, she will not shake hands with anybody, on the theory that germs of disease are conveyed in that way. She is extremely difficult to influence, owing to her ideas, and she lives a life of exclusiveness; in other words, she presents what one meets with in arterio-sclerosis at times. The cranium is conspicuously enlarged, the hypertrophy of the bone being the most marked on either side in the parieto-occipital region. The frontal bone is also prominent. The head gives the impression of being too large for the face. The patient is not aware of this enlarge-

[1] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1896.

ment of her head, but I am told that it has existed for some twenty years (?). The cervico-dorsal spine is rigid, as if ankylosed. The long bones are small, as if atrophic, like the muscles, but not bent abnormally. She is free from pain and other symptoms, excepting that she is slightly deaf. The eyes were not examined. It was difficult to obtain a complete examination, which was, therefore, somewhat limited, and not as thorough as could be wished.

Whether such a case as this should be classified with hyperostosis' and not as an incomplete case of osteitis deformans, is difficult to answer in the absence of any fundamental criterion. The hypertrophy of the cranium without involvement of the long bones gives a striking resemblance to hyperostosis cranii, while the kyphosis and apparent ankylosis of the spine, giving the effect of a spondylitis deformans, the generally impaired nutrition, and the arterio-sclerosis, are suggestive at least of osteitis deformans.

Putnam, in his excellent monograph on hyperostosis cranii, somewhat summarily dismisses the question of the possible identity of this disease with Paget's, as do almost all writers on Paget's disease, on the ground that the latter affects the long bones and is a disease of advanced age. It seems to me that each succeeding writer passes over this question somewhat cursorily, without due consideration, as if the idea of non-identity were handed down as a transmittendum from the earlier writers.

In addition to Putnam's collection of fourteen cases of hyperostosis cranii, I have been able to find six others reported to date by Horsley,[1] Ellis,[2] Priestly,[3] Sattler,[4] Parker,[5] and Roberts,[6] respectively. These, with the above case of my own, make twenty-one.[7]

Of these twenty-one cases ten apparently began after thirty years of age, and four after forty; and, conversely, of Packard, Steele and Kirkbride's collection of sixty-six cases of osteitis deformans, in eleven the disease began before the age of forty. Moizard and Bourges report a case in which the onset occurred at twenty-one years, and Blanc reports one beginning at seventeen years, but in this last the accuracy

[1] Practitioner, London, 1895, iv. 12–25.

[2] Archives of Ophthalmology, 1899, xxviii. 4.

[3] Quarterly Medical Journal, Sheffield, 1898, vii. 154.

[4] Cincinnati Lancet-Clinic, 1897, and Transactions of the American Ophthalmological Society, 1900. In the second paper the autopsy is reported.

[5] Annals of Surgery, 1894.

[6] Ibid., 1896.

[7] Ten other cases described under this title are to be found in the literature, but with insufficient evidence of the nature of the disease. Under a hyperostosis cranii a variety of diseases has been included from mere local tumors to a diffused condition, which later observation has shown to be osteitis deformans or some other process. In the absence of any definite criterion, I have been perhaps somewhat arbitrary in the exclusion of questionable cases. Perhaps future investigations may show that some of these may be varieties of the disease in question, but at present it would seem to be wiser to limit our study to typical cases. I, therefore, only include those cases in which the bones of the head have been more or less diffusely affected.

of the diagnosis is not above suspicion. At any rate, considering the small number of cases of hyperostosis cranii on record, the age limit seems to be hardly a sufficient criterion.

As to the non-involvement of the *long bones*, Bowlby and Edmunds have each reported a case claiming to be osteitis deformans in which only one long bone was affected, and Hutchinson a case in which only two long bones were affected. In Bowlby's case the histological examination showed changes resembling those described by Paget, so that if the disease may be limited to one bone it is logically possible that it may be limited to the cranium, which is so often and early affected.

It has been argued that a distinction between the two diseases is to be found in the hypertrophy of the malar bones in hyperostosis cranii giving the leonine appearance (leontiasis ossia), but this is not always found in this disease, and, conversely, I find that a careful examination of recorded cases shows that the bones of the upper face are not always unaffected in Paget's disease. For example, besides minor hypertrophic changes, like hypertrophy of the superior alveolar border found by Joncheray[1] and Meunier,[2] and of the inferior orbital arches in two cases recorded by Lunn,[3] Meunier found hypertrophy of the malar bones giving the appearance of leontiasis ossia in a typical case of osteitis deformans. Likewise, Gilles de la Tourette and Magdalaine[4] report a similar hypertrophy of the malar bones, as does Pic;[5] so that the presence or absence of this particular hypertrophy would not seem to have the importance ascribed to it.

From the point of view of pathological anatomy the differentiation of the two affections is equally difficult. In hyperostosis cranii the anatomical findings have consisted of new bone tissue in which calcification has taken place both in the surface layers and in the diploë, so that the latter is converted in some cases into a coral-like tissue; in others into a hard tissue like ivory, as was found in a case of my own. Actual softening does not seem to have been observed excepting in a case reported by Stack,[6] but I know of no case in which a histological examination was made, and, therefore, we can only surmise that, as in osteitis deformans, an absorptive process may have produced the sponge-like spaces in the hypertrophied diploë.[7]

Stack's case, which I have not included because it is not clear that

[1] Paris Thesis, 1893.
[2] Nouvelle Iconographie de la Salpêtrière, 1894, t. vii. 17.
[3] Trans. Clin. Soc., London, xviii. 273.
[4] Nouvelle Iconographie de la Salpêtrière, 1894, t. vii. 1.
[5] Rev. d'Orthopedie, May 1, 1897, viii. 164.
[6] Bristol M. C. J., 1900, xviii. 316-320.
[7] Four cases of Horsley's (Practitioner, 1895) reported under the title of leontiasis ossium ought not to be overlooked entirely. The hyperostosis was of the nature of a bone tumor, and was removed by operation. Histological examination of the removed bone in two showed the presence of a process which was both absorptive and osteoplastic.

it is not a complication of hyperostosis with osteomalacia, should be studied in this connection, for if softening of the long bones is not a complication the case is a transition between the two types we are considering. At the autopsy the skull was found to be enormously and almost uniformly thickened. All the cranial bones were affected, including those of the face. The cerebellar portion of the skull was very protuberant, dipping down toward the neck, and measured here in thickness almost three inches. The bones of the skull, on section, were for the most part softer than natural, but the appearance was not quite homogeneous. In parts there were masses of more compact tissue, and in others the rarefaction had proceeded to such an extent as to leave spaces of an eighth of an inch in diameter. The half skull without the lower jaw weighed seven pounds and a half. The lower jaw weighed one pound. The pelvis was very light, very soft, and much distorted; it was markedly generally contracted, scoliotic, funnel-shaped, and beaked. The femora were both bent and a little softer than natural. The tibiæ were also bent, and in some places the external compact layer was replaced by softened bone developed from the periosteum. There was no overgrowth in any bone apart from the head. It will be noticed that the rarefying process resembles in the description that of osteitis deformans.

Now, although in numerous histological examinations of the bones in osteitis deformans the findings have been similar to those described by Packard, Steele and Kirkbride, this would seem not to be the whole story, for more or less calcification may take place in the new bone tissue, so that patches of greater or less extent of ivory-like density occur.[1]

Not a few autopsy findings in which the formation of new bone with calcification is the chief process might be easily cited. The fact is,

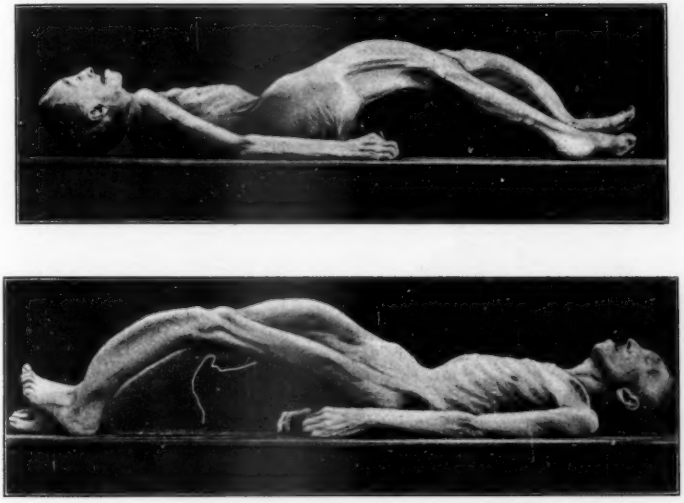
[1] Paget, in describing the findings in his first case, states that "the compact substance of the bones was in every part increased in thickness." "In the greater part of the walls the whole construction of the bone was altered into a hard, porous, or finely reticulated substance, like very fine coral. In some places, especially in the walls of the femur, there were small, ill-defined patches of pale, dense, and hard bone looking as solid as brick. In the compact covering of the articular ends of the long bones . . . the increase of thickness was due to encroachment on the cancellated texture, as if by filling its spaces with compact porous new-formed bone." Microscopic examination confirmed the macroscopic findings of new bone formation, with calcification. Bowlby describes similar changes in a femur, the only bone affected, remarking upon the formation of "new bone, sometimes of a hard, porcellanous appearance, and again of a more cancellous nature." Bowlby's case may be questioned as a true example, owing to only a single bone being affected, and yet the similarity of the changes to those found by Paget should be noted. Silcock, in an important observation, states that in a femur the superadded bone was everywhere compact and ivory-like excepting at one spot.

Lunn, again, while describing changes identical with those found by Packard, Steele and Kirkbride, also notes in addition the formation of calcified bone, which, as parallel lamellæ, reduced the size of the Haversian canals to the smallest calibre.

Equally important in showing calcification is the chemical analysis, which demonstrates substantially no deviation from the normal amount of lime salts in the bone (Paget) and even an increase (Robin, Gilles de la Tourette, and Magdalaine).

whether absorption predominates or new bone formation without calcification or with calcification, is probably either a matter of stage in the process or dependent on unknown determining factors. At any rate, as a matter of observation, one process may predominate in one bone and the other process in another in the same case. The autopsies, then, thus far made describe a combination of anatomical processes which may be briefly stated to be: (*a*) Absorption of bone; (*b*) new formation of bone tissue without calcification; (*c*) new formation of bone tissue with calcification. Any of these processes may predominate.

FIG. 5.



Sophia D., aged 73. Osteitis deformans. From a photograph kindly sent me by Mr. J. R. Lunn, F.R.C.S.

It is an interesting fact, to which attention has not been called in this connection, that in young, healthy growing bones an allied process takes place. The bone tissue around the Haversian canals may be absorbed, as in osteitis deformans, even to the extent of producing "irregularly bounded cavities of varying size with eroded edges, and lamellæ appearing as though gnawed away at points." Thus are formed the Haversian spaces. Reformation of new bone may then take place and fill up these spaces (Frey's *Histology*). This process is plainly a normal trophic one. This would suggest that it is within the bounds of possibility that the process in osteitis deformans is a modification or perversion of the same process which is provided for by nature in

normal bones. Under such an hypothesis it would be a nutritive or trophic disorder.

In hyperostosis cranii it is possible that the anatomical process may be the same as in osteitis deformans, only that the process of calcification has predominated, and hence the greater density of the bones of those skulls examined in this disease as compared with the bones examined in osteitis deformans. But it must be borne in mind that very few cases of hyperostosis cranii observed during life have come to

FIG. 6. FIG. 7.

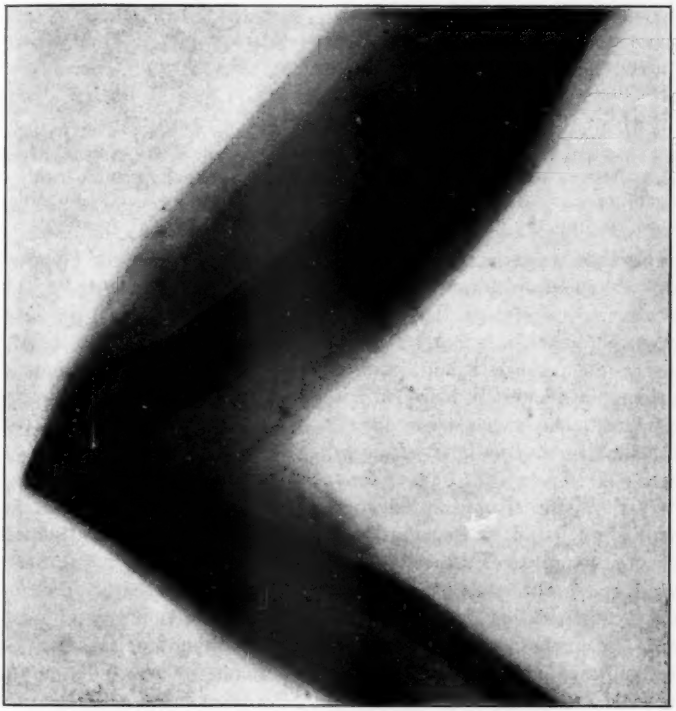
FIG. 6.—CASE III. Mrs. W., 1896. From Edes' article.
FIG. 7.—CASE III. Mrs. W., 1902. Osteitis deformans, formerly thought to be hyperostosis cranii. Compare with Fig. 6, which is the same case photographed in 1896.

an autopsy, and of these none have been submitted to microscopic examination, and in none, unless Stack's can be accepted, have any of the long bones been examined either macroscopically or microscopically, so that, after all, we have no positive knowledge that the long bones have not to some degree participated in the process. Then, too, in Paget's disease very few bones in any one case have been histologically examined; but, as the facts stand, of the bones examined in the same case one or the other has shown considerable calcification, while another has shown less. The evidence thus far is too fragmentary

to allow us to form a definite conclusion based on the anatomical findings alone.

CASE III.—Since the above was written I had an opportunity, through the kindness of Dr. Edes, to re-examine the case which he reported in 1896[1] under the title of hyperostosis cranii. I find that this case has developed into one of Paget's disease. Since 1896 the

FIG. 8.



CASE III. Osteitis deformans; right arm.

hypertrophic process in the head has greatly increased, as may be seen by comparing the photographs. (Figs. 6 and 7.) *Almost all, if not all, the long bones of the body are affected.* The right humerus is particularly deformed in a characteristic way, as is shown in the accompanying skiagram. (Fig. 8.) There is kyphosis in the lower dorsal region and deformity of the sternum. The clavicles have

[1] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, July, 1896.

escaped. The attitude of the patient is characteristic. What is of particular interest is that some of the phalanges of the fingers show traces of the disease in that they are bent, and the bones of the tarsus of one foot appear to be thickened. Then the nervous system shows certain abnormalities. There is general myasthenia, amounting to a paresis. The gait is paretic and unsteady, so that she requires help to maintain her balance in walking. She has a tendency to fall, not due to paresis, but no true ataxia can be made out, and Romberg's symptom is absent. The tactile and pain senses are normal; the knee-jerks are exaggerated. Plantar reflexes are absent. She has marked difficulty in swallowing, so that, for example, a glass of milk was drunk with great slowness and caution. The tongue protrudes straight; the face moves more to the right than to the left in speaking. The eyes are protruding, and there is a twitching of the right upper eyelid. There is decided deafness. There is no evidence of arterial atheroma, but there is an aortic systolic murmur. It is difficult to ascertain the exact time of development of the disease in the long bones. The patient says that her own attention was not called to these changes until after she had been observed by Dr. Edes, who tells me that he does not remember having made an examination of the limbs. It is possible, therefore, that the long bones may have been affected before 1896.

This case suggests the possibility that some of the other reported cases of hyperostosis cranii either may have developed later into Paget's disease, or that, if they had been more critically examined, the long bones would have been found to have been affected. As a matter of fact, in very few instances is any specific reference to the long bones made in the reports, and it is doubtful if they have been often examined. No reference to the long bones is made in Putnam's observations, and it is probable that they were not examined, as they were not in my own first case.

Osteo-arthritic Changes. The frequency with which osteo-arthritic changes are found in Paget's disease has not received the attention which they invite. These changes are identical in character with those found in certain types of rheumatoid arthritis, or, perhaps more correctly, osteo-arthritis. They are always regarded as evidences of coexisting rheumatoid arthritis rather than as different manifestations of the main pathological process. There are many facts which tend to show the incorrectness of this view.

In the first place, the frequency with which osteo-arthritic changes occur suggests some sort of kinship between this process and that in the body of the bones rather than the coincidence of two separate diseases.

Richard pointed out what he called transition cases between the two diseases. Humphrey calls particular attention to the presence of the two diseases in his specimens of a femur and tibia, as does Bowlby, who, in describing the appearance of the femur already referred to, specifically states that "some parts of the head and neck present changes exactly similar to those noted in an early stage of rheuma-

toid arthritis, the bone being smooth and porcellanous, with growth of nodosteophytes and with the worm-eaten appearance so common in this disease." In one of Stilling's cases von Recklinghausen found arthritis deformans at the autopsy. Goodhardt, in one case, describes deposits of new bone along the bodies of the vertebræ anteriorly, resembling in the description spondylitis deformans. In another case Goodhardt states that "bones of hard new-growth projected slightly from the substance of the bodies and welded the bones together by a tough, tuberculated mass, which looks not unlike the nodular masses found in some extreme cases of osteo-arthritis when that disease attacks the spine." Equally if not more remarkable findings in this particular, however, are those of Lunn, who describes a condition of the vertebræ exactly similar to that characteristic of spondylitis deformans of the type we are considering. "Projecting from the sides of some of the bodies of the vertebræ (chiefly lumbar) were well-marked bosses of new bone with disappearance of the intervertebral disks, and bony ankylosis had taken place at different intervals."[1]

The rigidity and ankylosis of the spine, which clinically is frequently observed in Paget's disease, undoubtedly is often, though not necessarily, due to a condition identical with that found by Goodhardt and Lunn, and described by Goldthwait in his monograph referred to. Clinically, also, ankylosis of the larger joints is not infrequently observed in Paget's disease, a process which is hard to explain by the absorptive and formative processes peculiar to osteitis deformans proper, and is probably due to the osteo-arthritic processes found at autopsies.

In my case nodosities are present in some of the phalangeal articulations, strongly suggestive of osteo-arthritis. In three of Lunn's cases ankylosis of the larger joints was present, and in a fourth there were bony growths about the knee-joints.

When we consider the variations in the anatomical processes found in osteitis deformans, there does not seem to be any good reason for regarding these osteo-arthritic changes as anything more than a predominance of the hypertrophic process which is observed in the bodies of the bones—a view which will receive support when we come to consider the disease as a trophic derangement.

In hyperostosis cranii, as well as in Paget's disease, the vertebræ sometimes take part in the hypertrophic process, or at least this seems to be the case from what can be made out during life. At any rate,

[1] Compare this with the following description of Goldthwait from his article on "Spondylitis Deformans, or the Spinal Form of Osteo-arthritis:" "Pathologically, the disease consists of a nodular enlargement of the edges of the articular cartilages, with the subsequent ossification of these nodes and an extension of the process into the ligaments which have their origin or insertion near by. With this hypertrophy at the edges of the cartilage the centres or areas of pressure usually undergo atrophy." . . . "As the process continues either the two surfaces of bone fuse or remain in apposition."

fixation of the spine (my case) and thickening of the vertebræ can be felt (Starr).

Special Pathology. Baumgarten, Starr, and Putnam have insisted that hyperostosis cranii is a trophic disorder, while several writers have done the same for Paget's disease. The thought suggests itself whether all the bone lesions commonly found associated in osteitis deformans and hyperostosis cranii, including those referred to rheumatoid arthritis, different as these anatomical lesions are, may not represent only perversions of a central trophic arrangement analogous to the so-called trophic lesions observed in spinal and nerve lesions. But when we attempt to point to any particular derangement, whether in the nervous system or elsewhere, we are made conscious of the blindness of our knowledge. And yet there are a number of facts which may have a bearing at least on the solution of the problem. So far as concerns the possibility of a central nervous derangement producing the osseous changes, the lesions in tabes and syringomyelia are instructive. In these diseases as well as some others affecting the central gray matter there is a very remarkable tendency to calcification or ossification of the ligaments and absorption of the cartilages of joints and development of bony masses about them—changes which in themselves have a very close resemblance at least to what occurs in osteoarthritis. Then, again, the process may be one of rarefaction or hypertrophy, and either may predominate. In the latter case the shaft of a long bone may undergo an extraordinary increase in size by the development of new osseous tissue on the surface. Further than this, deformities of the skull occur in syringomyelia, characterized by bossing of the frontal and parietal eminences and prominence of the forehead.

A very remarkable case was published by Hale White,[1] under the title of "Hyperostosis Cranii." Later the case came to autopsy as the result of operation for fits, and was described by Collier. Unexpectedly a condition of syringomyelia[2] was found, which did not give rise to the ordinary sensory symptoms of that disease, although there was a spastic atrophic paralysis of one arm of obscure origin, but thought before death to be cerebral. The skull was very remarkable. The deformity which had been taken for a hyperostosis was a projecting ridge or fold extending from the temporal region on each side backward around the occiput and overhanging the neck. It was as if the

[1] British Medical Journal, 1896, vi. 1377.

[2] Lancet, January 5, 1901. The cavity extended from the left inferior olivary downward in the posterior horn to the sixth dorsal, excepting that it intermitted from 8 c. to D 4; marked old degeneration in the right pyramid (tract?), which could be traced to lumbar region. Nerve cells normal by Nissl method; brain normal. Report too incomplete to allow cause of arm paralysis to be determined.

spine and base had been telescoped into the skull, which overhung the base like a mushroom.

The bones of the skull were for the most part small, and in some places thin, but in other places they were "unduly large" (hypertrophied?). The deformity had begun in childhood, and was supposed to have followed a fall upon the head.

The nature of the bone changes is not clear, but it was apparently one of perverted nutrition, and very likely connected with the syringomyelia as one of the trophic lesions of that disease.

The combined anatomical picture presented by these lesions in nervous diseases is very different, of course, from that seen in Paget's disease, but the individual processes suggest the variety of changes which may be brought about by one and the same nervous derangement. Several writers have suggested that the *fons et origo* of Paget's disease was to be found in the nervous system. Stilling, in 1889, attributed the coexistence of the two diseases to coincidence, and this view has been repeated successively by later writers. The possible dependence of osteitis deformans upon some kind of nervous lesion, it seems to me, has been rather hastily discarded without due consideration of the facts, and perhaps without a critical examination of the original records. Sometimes it has been taken for granted that the autopsy findings have negatived such an hypothesis. One of the later monographs states that "the results of many examinations . . . have shown the cord and bone nerves . . . to be perfectly normal." . . . This seems to be a hardly well-considered statement. I have not been able to find that the spinal cord has been examined at all, excepting in ten cases, and in five of these there was more or less evidence of pathological changes. In three (Gilles de la Tourette and Marinesco two, Levi one) a gross lesion in the form of posterior sclerosis was found under the microscope. In one, that of Pic, the spinal cord, to the naked eye, showed a grayish tint in the two posterior columns and in the right pyramidal tract. In one case (Stilling) some, though not marked, changes were found by von Recklinghausen, viz.: There was a small gliomatous growth in the cervical region and sclerosis of the ependyma. To the naked eye the gray substance throughout the whole length of the cord was white, opaque, and not easily distinguishable. The import of this is not mentioned by the reporter, but the ganglion cells and nerve trunks under the microscope appeared to be normal. It is suggestive that this case exhibited contractures and muscular weakness, if not paralysis, which must have been of spinal origin. In the sixth case, that of Lunn,[1] the spinal cord was found to be "soft in the cervical region, almost pulpy opposite the first and second dorsal and seventh cervical vertebræ."

[1] Transactions of the Clinical Society, vol. xviii.

"A year before the patient died he developed symptoms of bulbar paralysis, with extreme wasting of the tongue, dysphagia, and some loss of taste." *No microscopic examination was made.* It was evident that the cord softening, from its situation, was something in addition to the bulbar disease.

This leaves four cases to be accounted for. In two of these four (Stilling, Noizard, and Bourges) there was no microscopic examination of cord or nerves at all; but in the remaining cases, two, the microscopic examination showed the cord and nerves to be normal. Of ten cases, then, there was more or less good evidence of disease in six, not examined microscopically in two, and normal in two only. It does not appear that in either of the normal cases (Stilling and Goodhardt) any of the finer methods of technique were employed, including the special stains. One was examined as far back as 1878 (Goodhardt). The report of this simply states that " the spinal cord was quite healthy, both to the eye and under the microscope." The nerves were not examined. We must also bear in mind that we do not know what cells or elements in the cord, if any, regulate the nutrition of the bones, so that we do not even know where to look for the lesions which may be responsible for bone and arthritic changes. Therefore, it may well be easy to overlook them, as, indeed, the history of many originally obscure nervous diseases shows. At any rate, from this examination of the reports of autopsies it would appear that the frequency with which changes have been found in the nervous system has been overlooked. More opposed to the nervous origin of the disease is the fact of entire absence of nervous symptoms in the mass of cases; but this objection, it seems to me, is based on a too superficial view of the question. In the first place, as I have said, we know almost nothing of the seat of the trophic functions of the cord beyond the fact that lesions of the anterior cornua lead to muscular atrophy, and we are entirely ignorant of what elements in the cord subserve nutrition of bone or skin and other organs. Even in tabes we are ignorant of the special lesion which causes the trophic changes in the bones, whether seated in the anterior or posterior portions or in the peripheral nerves. *It is not inconceivable that as degeneration of the anterior cornua may cause myopathies without other symptoms, so lesions of other special cell groups may cause osteopathies without other spinal symptoms.* In the second place, it is a curious but interesting fact that in neither of the two cases of Gilles de la Tourette nor in that of Levi, in all of which an extensive sclerosis was found, were there any recognizable nervous symptoms during life, not even absence of knee-jerks, excepting that in Levi's case there was diminution of intelligence, ready weeping, and binocular nystagmus, and at the end only incontinence of urine and feces.

But it is exceedingly improbable that the lesion, if it is to be found

in the nervous system, is that of one of the stock nervous diseases. If such were the case we should expect to find the bone lesions occurring from time to time as manifestations of one or more of these diseases. It is much more probable that the pathological changes may be of a more general and finer type, such as would interfere with nutrition alone. Perhaps the arterial sclerosis which almost always is found, and which sometimes is so extraordinarily obtrusive in the younger cases, may be the primary source of nutritional changes. In the first of Gilles de la Tourette and Marinesco's cases the sclerosis of the posterior columns did not extend below the dorsal cord (the cervical cord was overlooked), and some of the fibres in the lateral columns were diseased. (The nerves were not examined.) In the second case, beside the sclerosis of the posterior columns most developed in the dorsal region, the peripheral nerves were the seat of an interstitial neuritis. The authors do not consider that the disease in the cord was a true posterior sclerosis, but rather an atrophy of nerve fibres. Levi also insists that the extensive sclerotic changes, with disappearance of myeline fibres, that he found in both posterior and lateral columns and other regions were to be regarded as a pseudosystemic sclerosis of vascular origin. The vessels throughout were the seat of a periarteritis and endarteritis. The spinal nerves showed irregular thickening of their connective tissues; the sciatic showed practically the same changes that were found in the cord.

It would seem to be highly possible that as a result, not of a posterior sclerosis or a lateral sclerosis, but of the vascular sclerotic changes that are always or almost always found in osteitis deformans, nutritional impairment might be brought about in the central nervous arrangements which we have to suppose govern the nutrition of the bones, just as the anterior cornua govern the muscles, and that future researches may reveal the nature and seat of these changes. In emphasizing this hypothesis I do not overlook the fact that in old people changes in the nervous system are apt to develop, and that the occurrence of these changes with bone lesions may be a coincidence.

What I have said is mostly speculative, but, considering the absolute blindness of our knowledge of osteitis deformans and the completely negative position in which this subject has been left by all writers on the subject, I have thought it might not be without value to put together the allied facts in our possession, hoping that they might furnish a working hypothesis and point the way for further pathological investigation, by which alone we can understand this most remarkable disease.

By way of summary, then, I would say:

1. We have no sure ground for differentiating hyperostosis cranii from osteitis deformans,

2. Hyperostosis cranii and osteitis deformans are probably trophic disorders.

3. Various clinical and pathological facts seem to indicate that they are at least allied disorders, and perhaps only different manifestations of one and the same disease.

4. The osteo-arthritic changes so commonly found in osteitis deformans are probably manifestations of the disease, and not complications.

5. The results of autopsies thus far made do not at all exclude the nervous system as the seat of the trophic derangement, but the changes that have been found in the spinal cord and peripheral nerves and analogy with other known lesions like those of tabes and syringomyelia suggest a neuropathic origin similar to that of the myopathies.

6. In future cases the nervous system should be exhaustively studied.

[NOTE.—I wish to express my obligation to Dr. Packard for his great kindness in loaning me his references to the literature and abstracts of reported cases, thus materially aiding this study.]

CERTAIN CHARACTERISTICS OF OSTEITIS DEFORMANS.

BY REGINALD H. FITZ, M.D.,
OF BOSTON.

THE first case reported by Dr. Prince subsequently came under my care at the Massachusetts General Hospital, having been referred to me by Dr. M. A. Morris, of Boston. There are certain points of interest resulting from my study of the patient and the disease concerned which I desire to place on record, even at the risk of duplicating some of the observations which Dr. Prince may have made.

These concern especially the recognition, by means of the Röntgen rays, of the alterations of the bones and the intimacy of the relation between cranial hyperostosis and osteitis deformans.

In this connection I wish to acknowledge my indebtedness to Mr. Walter Dodd, of the hospital, for the photographs and skiagraphs which will illustrate my remarks, and especially for his expert assistance in the interpretation of doubtful points in the latter series of pictures and in establishing the conclusions to be drawn from them. I am indebted also to my assistant, Dr. R. F. Gibson, for his aid in obtaining the completest possible record of the case, which is offered as a supplement to that of Dr. Prince.

The patient was born in Boston, in and near which she has always lived. Entered the Massachusetts General Hospital February 6, 1902. Her father died of phthisis, aged eighty-four years; her mother died

of the same disease at fifty-eight. Has two sisters, of thirty and thirty-eight years, respectively; both well. Has four living, healthy children. One died of unknown cause soon after birth. Has had measles, scarlet fever, and whooping-cough early in life, and seven years ago states that she had typhoid fever. Menopause at thirty-six. Has not used alcohol, but drank much tea until a year ago. Her average weight is 110 pounds.

Two years ago, when in her usual health, it was noticed that the right forearm was curved, and she attributed this condition to wringing clothes in her laundry work. A year ago, while walking, had three or four attacks of vertigo, each lasting a few minutes. These ceased at the end of a fortnight. Ten months ago she began to feel weak and tired, and had occasional periods of drowsiness. At this time there was slight, constant pain at the top of the head and in the occiput. She was able, however, to keep at work.

Five months ago, at the Boston City Hospital, she came under the observation of Dr. M. Prince, who first made her conscious of any peculiarity in her appearance, which, in her own opinion, has not since changed.

In January, 1902, she consulted Dr. M. A. Morris, of Boston, in consequence of severe pains throughout the head of some six weeks' duration, although temporarily replaced for a day or two on one occasion by pains in the left shoulder and hypochondrium. She complained also of digestive disturbances, which had been more or less troublesome for three or four months. At this time she considered her strength unaffected. Dr. Morris recognized her condition as one of osteitis deformans, and referred her to me, with the view that she should receive such opportunity for study and observation as the hospital might afford, and that she might attract the attention of medical students.

At the time of her entrance she complained of pain throughout the head and of sharp, shooting pains in the back, hips, arms, and legs. She was disturbed by gas in the stomach and bowels after meals. Pulse, 100; respiration, 20; temperature, 98° F. Weight, 99 pounds.

The cranium appeared large in all diameters, especially from before backward and from above downward. The occiput bulged and the temporal ridges were extremely prominent. The mastoid portion of the temporal bones was conspicuously large. There was marked enlargement of both malar bones and of the right lower jawbone. The other bones of the face were not enlarged. The hair of the scalp was coarse and dry, and bald spots were numerous.

Many of the teeth were gone from the upper jaw and several from the lower jaw. Caries was frequent in those present. The temporal arteries were markedly tortuous and thickened, and lay upon the surface of the bone.

There was pronounced kyphosis, with inability to straighten the curved portion, although elsewhere there was fair motion of the spine. The patient was pigeon-breasted, and the xiphoid cartilage was thickened and unyielding. The right clavicle was slightly enlarged, and there was enlargement of the acromion process and the spine of the right scapula. The crests of both iliac bones were thickened. There was some thickening of the right humerus and extensive upward and backward curvature, with thickening of both bones of the right forearm, the pronation of which was limited. The distal phalanges of each

hand were somewhat thickened. There was extensive thickening of both thigh bones, with curvature forward and outward. Both tibiæ, especially in the upper third, were decidedly thickened, and were curved forward, a change more marked in the right than in the left leg. The epiphyses were enlarged, the motion of the joints was not impaired, and there has never been any complaint of pain or stiffness in any joint or tenderness in any bone.

The following measurements were made by Dr. Gibson: Height, 57 inches; circumference of head, 24½ inches; distance from zygoma to zygoma over top of head, 13 inches; breadth between temples, 4¼ inches; distance from root of nose to point of chin, 4⅜ inches. Girth of right arm 3 inches above bend of elbow, 7⅝ inches; girth of left arm 3 inches above bend of elbow, 7½ inches; girth of right forearm 3 inches below epicondyle, 7½ inches; girth of left forearm 3 inches below epicondyle, 7 inches; girth of right thigh 6 inches above upper edge of patella, 16 inches; girth of left thigh 6 inches above upper edge of patella, 15⅛ inches; girth of right calf 5½ inches below lower edge of patella, 12½ inches; girth of left calf 5½ inches below lower edge of patella, 12½ inches.

The area of cardiac dulness was somewhat enlarged both to the left and right of the sternum. The apex-beat was diffused and heaving, most marked in the left fifth interspace 3½ inches from the median line. There was a systolic murmur in the aortic area, transmitted into the neck, and a harsh, systolic murmur in the mitral area, replacing the first sound and transmitted toward the axilla. The pulmonic second sound was accentuated. The action of the heart was somewhat irregular in force and rhythm. The radial arteries were thickened and ribbed, and the brachial arteries were thickened and tortuous. The volume and tension of the pulse were good in the right wrist, but diminished and obtained with difficulty in the left wrist.

The examination of the blood showed 80 per cent. of hæmoglobin, 4,450,000 red corpuscles, and from 7000 to 10,000 leucocytes. The differential count of the latter gave 70 per cent. of polynuclear leucocytes, 18 per cent. of small, and 4 per cent. of large lymphocytes.

The examination of the lungs and abdominal organs was negative. The urine was acid, 1020, contained neither albumin nor sugar, and the sediment was not pathological. At one examination, however, the slightest possible trace of albumin and a rare granular cast were found. The pharyngeal reflex was absent, but the pupillary, patellar, and plantar reflexes were present and normal.

The eyesight had been failing somewhat for the past two years, and glasses have been worn with relief for five months. There is no impairment of hearing. The sense of touch is unaffected; there are no paræsthesiæ, and the appreciation of heat and cold is normal. There is less sweating than formerly, but the skin is soft and smooth. The loss of hair began nine months ago, and persisted for six months; she thinks that nearly one-half is gone. There is no loss of hair except from the scalp. The finger-nails show no alteration.

When the patient entered the hospital there was an evident impairment of mental function; her answers were intelligent and direct, but at the end of three days she left her bed at night and wandered from the ward, expressing fear that her eyes were to be taken out; the latter had been examined ophthalmoscopically a day or two before. She

remained in the hospital nearly four weeks. During this time she gained some four pounds in weight, her pains lessened, but she was more or less restless at night, at times screaming or attempting to leave the ward, or threatening to injure herself in consequence of delusions with regard to her children. She believed them dead, and when visited by them stated that the visitors merely simulated the children, although wearing their clothes. She heard imaginary conversations, and complained that the nurse did not give the right medicine and lied about her. She thought some dreaded operation was to be performed, wept occasionally, and talked constantly about her troubles and ailments. In consequence of the persistence of her delusions and the inability of her family to take care of her she was transferred to the Boston Lunatic Hospital.

To recapitulate: A healthy, hardworking woman at the age of forty-three years became aware of a curvature in the right forearm. A year later there were temporary attacks of vertigo for a short time, which soon were followed by pains in the head, drowsiness, and debility. Five months afterward her cranial deformity was first called to her attention. At present there is hyperostosis of the cranium, malar bones, right inferior maxilla, clavicle, scapula, humerus, radius, ulna, iliac crests, femora, and tibia. There were also kyphosis and pigeon-breast.

The case evidently is one of osteitis deformans, with conspicuous cranial hyperostosis complicated with rheumatoid arthritis, arterial degeneration, chronic valvular disease, and, lastly, with mild melancholia accompanied with delusions.

The alterations of the bones in osteitis deformans, originally described by Paget,[1] are recognized as characteristic by later observers, and nothing essential has been added to his statement of them. The bones usually affected are those of the cranial vault, the spine, and the larger long bones of the extremities; less frequently the clavicles, scapulæ, ribs, sternum, and pelvis are altered, and, rarest of all, is mention made of changes in the bones of the face, hands, and feet. The enlarged bones are abnormally dense or rarefied. The surface is smooth or rough, nodular or protuberant; the cortex thickened or thinned, spongy or eburnated, the cancellated structure sclerosed or coarsely trabeculated, the marrow spaces obliterated or transformed into cavities of various sizes. The central canal of the long bones is narrowed or dilated, even to disappearance, and the deformity of these bones is further increased by various degrees of abnormal curvature. There is no uniformity in the distribution of these alterations, and a single bone may give evidence of the decalcification and absorption, the formation of osteoid tissue and its calcification, which are the processes concerned in the production of the gross changes. Multiplicity of the bones affected is the constant characteristic.

Until within the past few years the closer study of the nature and distribution of these changes has been possible only by the examina-

[1] Med.-Chir. Trans., 1877, lx. 87.

tion of macerated bones and by the microscopic investigation of decalcified portions of certain bones. The information thus obtained is somewhat fragmentary, and necessarily limited to the conditions existing at a particular time, although early and late manifestations of the disease may be present at one and the same time. All writers call attention to the unknown period of latency, during which the existence of the malady is unrecognized, and the long term of years through which it slowly progresses. Any means by which periodical examinations of the alterations in the bones may be made promises to add very materially to our knowledge of the subject, especially with reference to the progress of the affection and to the conditions promoting curvature, and the future study of osteitis deformans and allied diseases in

FIG. 1.

Hyperostosis of first phalanx of thumb, fourth metacarpal and carpal end of radius. Osteoarthritis of terminal phalanges. Calcification of arteries of arm and hand.

which the bones are involved must depend largely upon the use of the Röntgen rays. Watson,[1] Elting,[2] and Wilson[3] already have illustrated their communications on osteitis deformans with skiagraphs. These show the degrees of enlargement and curvature of certain bones, and Watson in particular calls attention to peculiarities of structure. The accompanying skiagraphs, made by Mr. Dodd, still more satisfactorily indicate the value to be anticipated from the use of the Röntgen rays in defining the various stages in the progress of the disease, and they are contrasted with those obtained from normal bones for the purpose

[1] Johns Hopkins Hospital Bulletin, 1898, 133.
[2] Ibid., 1901, 343.
[3] Philadelphia Medical Journal, 1902, ix. 322.

of ready comparison. They are a portion only of the series taken. (See Figs. 1–11.)

Mr. Dodd describes the alterations as follows:

"*Skull* much thickened, lower jaw greatly enlarged, coarse trabeculation and decalcification.

"*Clavicle* hyperostotic, the condition more marked in right than in left collar-bone.

"*Scapula.* Axillary border; acromion and coracoid process of right scapula hyperostotic, with foci of decalcification. A similar condition in the left scapula, but much less in degree.

"*Humeri* hyperostotic, with coarse trabeculation and decalcification. The alterations more extensive in the right than in the left humerus.

FIG. 2.

Normal hand.

FIG. 3.

Normal foot.

"*Forearm.* Right radius and ulna hypostatic, with decalcification; marked curvature of radius. Bones of the left forearm apparently normal.

"*Hands.* Terminal phalanges of each hand show the conditions found in osteo-arthritis. The right hand shows hyperostosis of the third metacarpal bone, with area of decalcification; also marked hyperostosis of carpal end of the radius and ulna. In the left hand there are hyperostosis of the first phalanx of the thumb and a spicule of bone (?) at the inner border The head and cortex of the fourth metacarpal bone apparently thickened.

"*Pelvis.* Hyperostosis and coarse trabeculation throughout the right os innominatum.

"*Right Femur.* Hyperostosis and coarse trabeculation throughout the shaft. The neck and head also involved, but to a less extent. Right patella also shows hyperostosis and coarse trabeculation.

"*Lower Leg.* Tibiæ hyperostotic, with coarse trabeculation and large areas of decalcification, more marked in the right than in the left tibia.

FIG. 4.

Right. Left.

Right. Hyperostosis of all metatarsal bones except the third. Foci of decalcification of first and third. Absence of trabecular structure in second contrasted with its persistence in the fifth metatarsal.

Left. Hyperostosis and decalcification of first phalanx of great toe. Hyperostosis and decalcification of all metatarsal bones except the fifth.

FIG. 5.

Right femur from inner lateral surface. Hyperostosis of femur, extending into epiphysis. Cortical thickening; erosion of anterior surface of femur. Hyperostosis of patella, decalcification and coarse trabeculation.

FIG. 6.

Normal.

Cortical thickening of the right tibia and fibula. Left internal malleolus almost wholly decalcified.

"*Foot* (*Right*). Hyperostosis and decalcification of the astragalus, os calcis, and all the metarsal bones except the third. Decalcification of the first and second metatarsal bones. Trabecular structure well preserved in the fifth, but absent in the first and second bones. The phalanges normal. The left foot shows hyperostosis of the astragalus,

FIG. 7.

Left ankle and lower two-thirds of leg. Hyperostosis and decalcification of the tibia, fibula, astragalus, and os calcis. Coarse trabeculation, lamellar thickening of tibia and fibula.

FIG. 8.

Normal ankle.

os calcis, cuboid, and internal cuneiform bones. Decalcification and coarse trabeculation are especially apparent in the os calcis. Hyperostosis of all the metatarsal bones except the fifth, which is apparently normal. The first phalanx of the great toe shows marked hyperostosis and decalcification. Other phalanges normal."

From the inspection of this series of skiagraphs it is evident that the various changes in the bones described by Paget are to be determined to a considerable degree in the living patient. The nature and extent of the involvement of individual bones is appreciable, likewise the discovery of similar changes in bones which hitherto have attracted but little attention, notably those of the hands and feet. It is obvious that if a series of such pictures could be taken from time to time and preserved a most graphic record of progress would be obtained.

The similarity of the changes of the skull in the affection designated hyperostosis cranii or leontiasis ossea, and in osteitis deformans has

repeatedly been observed, and Paget recognized the importance of discriminating between these affections. In the reported cases of cranial

FIG. 9.

Hyperostosis of tibia, astragalus, os calcis, cuboid, and internal cuneiform. Decalcification and coarse trabeculation especially apparent in os calcis.

FIG. 10.

Normal.

FIG. 11.

1. Normal. 2. Hyperostosis of both external malleoli; extensive decalcification; disappearance of right internal malleolus.

hyperostosis the alterations of the skull have sufficiently been described, but, unfortunately, little mention has been made of the condition of

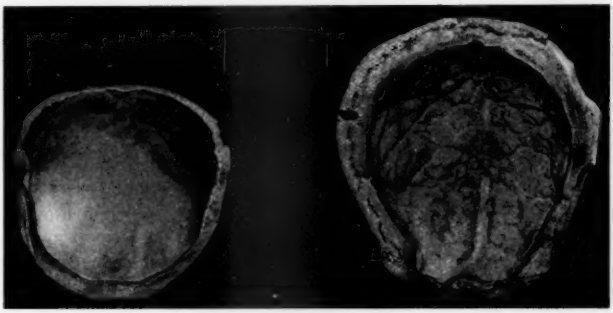
FIG. 12.

Osteitis syphilitica. Hyperostosis.

FIG. 13.

Osteitis syphilitica. Hyperostosis.

FIG. 14.



Osteitis syphilitica (?). Hyperostosis.

other bones. This omission was due in part to the preservation of the skull alone, in part to the less striking changes in other portions of the

body, perhaps from the early stage of their development, or because attention was not directed to their possible presence.

Within the past ten years renewed attention has been called to cranial hyperostosis, especially through the publications of Drs. M. Allen Starr, Putnam, Prince, and Edes. This disease usually is described as occurring early in life and as almost exclusively concerning the bones of the skull and face. The hyperostosis is frequently combined with sclerosis. The narrowing of foramina, fissures, and cavities and the deepening of canals are emphasized. Affections of sight and hearing, facial paralysis, difficulties in chewing, swallowing, and breathing are to be found among the disturbances, and the cerebral functions generally suffer.

Nevertheless, the difficulty of regarding cranial hyperostosis as an independent disease is repeatedly experienced. Baumgarten, in 1892, discussed the possible relation to Paget's disease, and M. Sternberg[1] admits that some of the cases described as cranial hyperostosis should be regarded as osteitis deformans. Atkinson[2] considers that the former is a manifestation of the latter. Crozer Griffith at the last meeting of the Association of American Physicians also expressed the opinion that a sharp separation between the two diseases is at present impossible. Cranial hyperostosis has appeared at a late period in life, and osteitis deformans is not limited to advanced years.

The failure to recognize bone lesions elsewhere in cranial hyperostosis is not necessarily due to their absence, and the case here reported by Dr. Prince and myself gives evidence that the bones of the face may be diseased in osteitis deformans. The skull brought to this country by Spurzheim, and now preserved in the Warren Museum of the Harvard Medical School, is usually regarded as an example of cranial hyperostosis, but shows the changes described as occurring in Paget's disease, while the skull of the case reported by Putnam as cranial hyperostosis shows extensive sclerosis, little or no rarefaction, and not much enlargement—alterations suggestive rather of syphilis than of Paget's disease. (See Figs. 12–14.) The presence of mental derangement cannot be regarded as of significance in the differential diagnosis, since our patient with Paget's disease eventually so suffered from delusions and loss of self-control as to require treatment in an asylum.

It would seem from the above considerations that hyperostosis is a condition which may affect few or many bones, early or late in life, and with inconstant symptoms; that the evidence in favor of the recognition of an independent disease—diffuse cranial hyperostosis—is insufficient, since the symptoms assigned to this affection are inconstant, and may occur in osteitis deformans.

[1] Nothnagel's Sp. Path. und Therap., 1899, vii. 22.
[2] Maryland Medical Journal, 1901, xliv. 281.

Finally, of the twelve reported cases which, according to M. Sternberg, serve as the basis of the clinical study of this affection, one at least, as shown by Dr. Prince, eventually proved to be an example of osteitis deformans, while the cranium of another, subsequently obtained by Dr. Putnam, showed lesions suggestive rather of syphilis than resembling those present in the hyperostotic skull from the Spurzheim collection, which correspond to those described by Paget as occurring in osteitis deformans.

VARIOUS OPERATIVE PROCEDURES FOR THE RELIEF OF CHRONIC SUPPURATIVE OTITIS MEDIA, AND THEIR COMPARATIVE VALUE.[1]

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A chronic suppurative otitis media may result from several conditions within the middle ear. In its simplest form it presents as a case of acute inflammation of the tympanic cavity in which the products of inflammation have been evacuated either by spontaneous rupture of the drum membrane or by incision of this structure, and in which the discharge simply continues for an indefinite period after the acute symptoms of inflammation, such as pain, etc., have passed away. Cases of this character could not, with propriety, be considered in this paper. Such a condition as that described usually requires no operative procedures upon the middle ear for its relief. This paper has to deal only with those cases in which the suppuration is of long standing and has persisted in spite of the ordinary measures usually undertaken for the relief of a simple aural discharge. By these I mean the enlargement of any opening already present in the drum membrane, the thorough cleansing of the parts, the preservation of asepsis in the canal, the relief of recurrent congestions of the upper air passages by proper surgical measures directed to this portion of the anatomy, and the institution of free drainage through the external canal by the removal of granulation tissue.

A chronic otorrhœa of the type under consideration always depends upon the presence of diseased bone within the tympanic cavity. The intratympanic caries may have resulted from an acute inflammation within the tympanum, the middle-ear condition having been neglected at the time of the acute attack, and bony destruction having occurred

[1] Read before the American Laryngological, Rhinological, and Otological Society, June, 1902, Washington, D. C.

before the evacuation of the inflammatory products of the middle ear by spontaneous rupture of the drum membrane. I think we may lay it down as a general rule, to which there are but few exceptions, that no matter how virulent is the primary infection, if the case is seen early in the acute stage, serious intratympanic caries can be prevented. The only exception that I would make to this statement are the cases in which we have early involvement of the mastoid cells following an acute inflammation within the middle ear; in other words, given an acute purulent otitis media which does not develop acute mastoid symptoms, intratympanic caries can be almost certainly prevented in such a case, provided the patient is seen within the first twenty-four or thirty-six hours of the attack.

In another class of cases, which are fortunately rare, the purulent otitis is due to a tubercular infection of the intratympanic structures. Here treatment in the early stages will probably be of no avail in preventing intratympanic caries, as this caries has generally occurred before the patient has the slightest suspicion that there is anything the matter with the ear and before he applies to his medical attendant for relief.

From what has gone before it is evident, therefore, that intratympanic caries or necrosis is the essential and underlying cause of the symptom, chronic otorrhœa. The surgeon must deal with the dead bone in the tympanic cavity in exactly the same way as he would deal with a similar condition in any other portion of the body. All foci of caries and necrosis must be removed, and free drainage must be established in order to further protect the patient against secondary infection and a later extension of the diseased process within the bone. The operation wound should be made to heal as rapidly as possible, and an attempt should be made to cover the bony surface with epidermis, in order that slight congestions of the upper-air tract may not cause a similar condition within the cavity of the tympanum, which in turn may be followed by a reinfection of the bony structures and an extension of the caries.

Two methods of procedure are open to the operator: The first, and the one which is ordinarily considered the more simple, is to remove all carious bone through the external auditory meatus. Knowing, as we do, that when intratympanic caries exists, in the early stages, it is usually confined to the ossicular chain and to those parts of the tympanum immediately adjacent to the malleus and incus, it seems reasonable to suppose that the removal of the malleus and incus and the thorough curettement of the middle ear through the external auditory canal should constitute an efficient procedure for the relief of a chronic otorrhœa in certain instances. We have abundant proof, both in our own experience and in that of others, that this is a fact.

It is perfectly possible, in performing an operation of this kind, to remove not only the ossicles, but also any carious bone situated low down in the tympanic vault. Where caries is confined to the ossicular chain alone the procedure already mentioned is the ideal one. The operation is not severe, and seldom confines the patient to the house for more than one or two days, and sometimes even for a shorter time. By the thorough use of the curette it is usually possible to destroy the mucous membrane lining the tympanic cavity and to secure a complete dermatization of the walls of the cavity. When this can be done the procedure is certainly an ideal one. In addition to the minimum amount of confinement to which the patient is subjected, it is almost always possible to avoid injury of important structures, either in the tympanum or adjacent to it. This is particularly important when we come to consider that any operation upon the middle ear having for its purpose the removal of certain structures within this cavity must constitute a certain menace to the power of audition. The simpler, then, the character of the procedure the less danger is there of interfering with the function of the organ. Moreover, this must be borne in mind: that injury to adjacent structures, such as the facial nerve, the jugular bulb, the semicircular canals, the cochlea, and the cranial contents, seldom occurs during the course of this simple operation.

In many cases, however, we have to deal with a caries of the middle ear so extensive that it is impossible to remove all diseased tissue through the narrow confines of the external auditory meatus. In these cases it is necessary to freely expose the tympanum and the adjacent pneumatic cells within the mastoid by the extensive removal of the osseous walls. In this way all diseased areas can be brought thoroughly under the eye of the operator, and every vestige of diseased bone can be removed. Such an operation involves the exposure of the bony auditory meatus by reflecting forward the fibrocartilaginous canal. The operative field is still further enlarged by the removal of the upper and posterior wall of the bony external auditory meatus at its inner extremity, thus throwing the tympanic vault and the lower portion of the cavity (that part covered by the tympanic membrane) together. Such a procedure constitutes the operation devised by Stacke,[1] and which has since borne his name.

In the cases where the mastoid cells are also involved it is necessary to make a still more extensive exposure. In these cases a typical mastoid operation is first performed. The mastoid antrum is opened as the first step of the procedure, after which the partition between the external auditory canal and the opening in the mastoid is broken down, thus throwing the tympanic cavity, the tympanic vault, the

[1] Archiv für Ohrenheilkunde, vol. xxxi. p. 201.

mastoid antrum and adjacent cells, and the external auditory meatus into one large cavity. This operation is known as the Stacke-Schwartze operation.

As I have stated many times in previous writings, the choice of operation in each individual case must depend upon the extent to which the bony structures are implicated. In those cases in which there is evidence that the intratympanic caries is limited to the ossicular chain, the simple operation of removal of the ossicles is undoubtedly indicated. Where, however, we have reason to believe that the disease has extended to the tympanic vault, the Stacke operation would seem the procedure of election. In all other cases, where the destruction of bone is extensive, the radical procedure, known as the Stacke-Schwartze operation, would be the procedure of choice. It would seem at first quite possible for the surgeon to make a differential diagnosis in these cases and in every instance to select the procedure advisable in each individual case presenting. I confess in previous years this has been my view, and that I have leaned very strongly to the simple operation of extraction of the ossicles, except in cases where there was abundant evidence of extensive involvement of the adjacent pneumatic structures. Later experience has led me to believe, however, that conservative surgery in this region is a mistake rather than an advantage. While I believe that the simple operation is indicated in a certain proportion of cases, I also believe that the field of this operation will become more and more restricted as the experience of the surgeon becomes wider.

Out of 92 cases operated upon by the author by removal of the ossicles and curettement of the tympanum, 53 were cured, 25 improved, 2 unimproved, and in 12 the result was unknown. The two cases recorded "unimproved" in the preceding statistics were subsequently operated upon by the Stacke method, while two which were reported as "improved" later required the same procedure, and were operated upon subsequently.

Grunert[1] reports the following results from ossiculectomy: of 28 cases, 13 were cured, 13 were not cured, and 2 were still under treatment at the time of the report.

Ludwig,[2] in two articles in which he deals very fully with the subject of middle-ear caries and the relief of the same by the extraction of the malleus and incus, reports[3] 43 cases operated upon in which he found that the suppuration was cured in 22 cases, the discharge continued in 5, 9 were still under treatment at the time of the report, in 5 the result was unknown, and in 2 cases the patients died, although the fatal issue was in no way attributable to the operation.

[1] Archiv für Ohrenheilkunde, vol. xxxiii. p. 222.
[2] Ibid., vol. xxix. p. 241, and vol. xxx. p. 263.
[3] Ibid., vol. xxx. p. 263.

Schroeder[1] reports 130 cases of extraction of the malleus and incus for middle-ear suppuration. Out of this number, 62 were cured, 39 were not cured, in 28 the result was unknown, and 1 was still under treatment at the time of the report. It should be stated that although these cases of Schroeder are reported as cases of extraction of the malleus and incus, in 19 cases the malleus alone was extracted, the operator being unable to find the incus. In 9 others neither the malleus nor incus could be found, presumably having been previously destroyed by caries, while in 3 cases it was necessary to stop the operation on account of profuse hemorrhage.

From the foregoing results it will be seen that out of Grunert's 28 cases, 46 per cent. were cured; in Ludwig's 43 cases, 51 per cent.; in Schroeder's 130 cases, 48 per cent.; while in the author's cases 57 per cent. were cured.

The variations in these statistics are so slight that the difference might easily occur from the class of cases which came under the observation of a certain operator. These statistics simply go to show that in a certain proportion of cases—that is, in at least one-half of the cases of suppurative otitis subjected to this operation—a cure resulted.

A few words may not be out of place in regard to the technique of the operation. From the first I have always insisted upon the absolute necessity of removing the incus in every case. Ludwig, in his masterly article on "Caries of the Ossicula," tells us that in at least 85 per cent. of all cases of intratympanic caries the incus was found diseased. It goes without saying, therefore, that the operator must make a thorough and complete search for the incus in every case. Even a small fragment of this ossicle remaining would be sufficient to cause the suppuration to continue indefinitely. While we have all of us met with cases in which it was impossible to find even a fragment of the incus, the operator should not consider his operation complete unless the incus, or what remains of it, is removed, or unless he has satisfied himself thoroughly that not even the smallest fragment of this ossicle remains. It has been my experience not infrequently to find a small fragment of the incus only after a persistent search, and it has been my invariable rule to prolong my operation almost indefinitely, in order to make certain that no remnant of this ossicle has been left behind. It is, perhaps, for this reason that the result in the cases which I have reported is slightly better than in those of the other operators. I would not be understood as saying that I have always found some portion of the incus in these operations. In quite a number of cases I have failed to find even the slightest trace of the ossicle, but I have only desisted from my search after a prolonged exploration in every portion

[1] Archiv für Ohrenheilkunde, vol. xlix. p. 17.

of the tympanic cavity accessible through the external auditory canal. It is impossible for me to report on my entire 92 cases, as I have not had sufficient time to look over all of my old histories. Moreover, in many of my earlier cases the records are incomplete. Out of the last 33 cases operated upon I find that in 23 cases the malleus and incus were removed, in 4 the incus was not found, and in 6 cases the history of the operation does not state whether one or both ossicles was removed.

Regarding the search for the incus, one point in the technique is to be remembered—that the ossicle lies close to the margin of the tympanic ring. After the malleus has been removed, the incus hook, with the curve looking forward, should be introduced low down into the canal, and should be made to enter the tympanum until its angular extremity disappears behind the posterior margin of the tympanic ring. The hook is then pulled outward until its angular portion engages upon the ring. The instrument is then swept upward toward the tympanic vault and at the same time rotated forward by the fingers, so that the incus, if present and not completely destroyed, will be engaged by this instrument and brought into the field of vision. It is necessary to repeat this manipulation several times in order to be certain that a small fragment of the incus is not lodged in the posterior and upper portion of the tympanic cavity. Too much force should not be used in carrying out this step of the operation, but, at the same time, sufficient force should be employed to break down any adhesions that may be present in the posterior part of the tympanic cavity, and, if the fragment of incus is perfectly encapsulated in dense connective-tissue bands, to break up these adhesions and dislocate the fragment of the ossicle forward and downward into the tympanum. Sometimes we find these bands so dense that the incus hook will not divide them. When this is the case the angular knife should be introduced into the tympanic cavity and swept upward and backward through the posterior and upper segment, so as to divide any connective-tissue bands which may be present in this locality. I have in quite a number of cases found a small fragment of the incus lying in a little pocket just at the junction of the upper and posterior wall of the meatus. In these cases, as we know, the long process of the incus is first destroyed, and the small remaining fragment of the body of the ossicle lies upon the little shelf which is formed by the inner extremity of the superior wall of the bony canal. In cases where the caries is of long standing, after the destruction of the long process of the incus, the body is frequently encapsulated in what appear to be the remnants of the capsular ligament, forming a mass of encapsulated tissue which has been thrown out around the body of the ossicle. This capsule is, as before stated, firmly adherent to the inner extremity of the canal wall, and frequently remnants of the capsule, together with the necrotic incus body, are swept down from

the shelf and extracted at the same time. After the incus hook has been used in the manner already described, and in cases where it is necessary the angular knife as well, if the operator fails to find any vestige of the ossicle it is well to explore the anterior and inferior portions of the tympanic cavity by means of the incus hook, lest the ossicle may have been dislocated downward and forward at the time that the malleus was removed, and have lodged in the antero-inferior portion of the cavity. To effect this the sweep of the incus hook is simply continued forward, through the tympanic vault, down to the tympanic floor, the hook being gradually rotated so that the curve at first looks forward, then backward, and then upward as the hook reaches the lower portion of the cavity. During this entire manipulation the angular portion of the hook should be pretty closely applied to the tympanic ring, so as to avoid injury of important structures upon the internal tympanic wall. A certain number of operators advise the use of the incus hook in a different manner—that is, the instrument is introduced into the canal with its concavity looking backward, and is swept from before backward and downward through the tympanic vault, so as to dislodge the ossicle downward and backward into the lower portion of the tympanic cavity. It can at once be seen that the use of the incus hook in this manner renders it exceedingly possible to dislocate a small fragment of the incus backward into the mastoid antrum or into the *aditus ad antrum*, where it will be beyond the reach of any instrument introduced into the canal.

Another point in the performance of the operation upon which I have always insisted is the perfect removal of the floor of the tympanic vault whenever this portion of the middle ear is diseased, and it is almost always diseased in cases of intratympanic caries.

The floor of the tympanic vault is best removed by a small pair of angular rongeur forceps, cutting antero-posteriorly, which are introduced through the speculum into the canal and made to bite away as much of the inner extremity of the superior bony wall as can be engaged between the blades. It is often wise to institute this procedure immediately after the removal of the malleus in those cases where a moderate search fails to reveal any trace of the incus. Not infrequently, after the removal of the floor of the tympanic vault in this way, a remaining fragment of the incus can be easily seen and extracted.

In addition to what has been said about the thorough search for the incus and the removal of the floor of the tympanic vault, no operator should feel that the operation is completed until the entire middle ear cavity has been thoroughly curetted. While intratympanic caries is sometimes limited to the ossicular chain, most frequently the tympanic walls are, to some extent, involved as well. It is necessary, there-

fore, to curette carefully not only the atrium and margins of the ring, but, by means of the angular curette, the tympanic vault as well, so as to remove every possible focus of diseased tissue. The curette should also be introduced well into the tympanic orifice of the Eustachian tube, so as to cause a closure of this tube if possible, to prevent subsequent infection of the middle ear from the nasopharynx.

While hemorrhage has in many of my cases prolonged the operation unpleasantly, I have never had a case of hemorrhage sufficiently severe to render it necessary for me to stop the operation. In one case, at the very last stroke of the curette, the jugular bulb was wounded. Had this accident occurred earlier in the operation I undoubtedly would not have been able to proceed further; but fortunately both the malleus and incus had been extracted, and the walls of the cavity had been pretty thoroughly curetted before the accident happened. I cannot conceive of hemorrhage sufficiently severe to cause the operator to desist from completing the operation, unless either the jugular bulb or the internal carotid should be accidentally injured. Of course, either accident is possible, as there may be dehiscences in the internal tympanic wall, either congenitally or as the result of a pathological process. All other hemorrhage can be easily controlled by packing the canal and middle ear firmly for a few moments with a strip of sterile gauze. For the last few years I have been in the habit of saturating these gauze strips in a sterilized solution of suprarenal extract, and have found that the hæmostatic effect of this drug materially aids the operator. The bleeding is very quickly checked, and the operation can be proceeded with much more rapidly than where simple packing alone is relied upon.

We now come to considering the so-called radical operation, first proposed by Stacke and since advocated by many prominent otologists. This procedure has already been somewhat roughly described in the early portion of this paper. The results obtained by the Stacke-Schwartze operation compare most favorably with those obtained by the simpler procedure. Out of 37 cases operated upon by the author, 27 were cured, 5 improved, 1 unimproved, 1 unknown, and 3 are still under treatment.

Panse,[1] in discussing the radical operation of which we are at present speaking, reports 57 cases operated upon; of these 31 were cured. Of the remaining cases the author simply states that they have not been under observation long enough after the operation to warrant a report as to their condition. These cases must therefore be looked upon as still under treatment.

Grunert[2] out of 43 cases operated upon by this method reports 24 cured, 18 either unimproved or still under treatment, and 1 death.

[1] Archiv für Ohrenheilkunde, vol. xxxiv. p. 248.

[2] Ibid., vol. xxxv. p. 198.

Regarding the technique of the radical operation, a few remarks may not be amiss. In the first place, the location of the incision through the soft parts is a matter of some importance. For a long time it has been my rule in making the incision in the ordinary mastoid operation to divide the soft tissues down to the bone just behind the line of auricular attachment. In this way the line of incision lies practically in the post-auricular fold, and the deformity caused by the incision is insignificant. In performing the radical operation now under consideration it is best to make the incision much further back. The soft parts should be divided by a curvilinear incision, which should lie at least five-sixteenths or, in some cases, one-half inch behind the line of auricular attachment. Some operators, notably Ballance,[1] prefer, in case the incision is made at a considerable distance from the ear—say half an inch behind the line of auricular attachment—to make this incision only through the integument and subcutaneous areolar tissue. The anterior flap is then dissected up for about a quarter of an inch, and the remaining soft parts are divided down to the bone. In this way the posterior flap is terraced, so to speak, to the margin of the bony external auditory meatus. Personal experience has taught me that there is not much advantage in making the flap in this way. It is, however, wise, to make the incision further back than is usually done in performing the ordinary mastoid operation.

After the soft tissues have been divided by either method the anterior flap is rapidly dissected forward until the posterior and upper margin of the bony meatus is exposed. The fibrocartilaginous meatus is then dissected out of the bony canal by means of a thin, narrow periosteal elevator, the dissection being carried as deeply as possible. The fibrocartilaginous tube will be found to rupture spontaneously close to the drum membrane. Forcible traction is now put upon the anterior flap, and the posterior, upper, and inferior aspects of the cartilaginous meatus are forcibly drawn forward by means of such traction, so as to expose the bony meatus along the superior, posterior, and inferior aspect. If firm traction is applied to the anterior flap the operator will be able to look directly upon the external wall of the middle ear—that is, upon the drum membrane or its remnant. Sometimes the posterior wall of the fibrous meatus is very much thickened, and on retraction of the anterior flap it may be projected backward across the bony meatus, so as to somewhat obscure the view. Under these circumstances it is well to thread a broad strip of sterile gauze through the external auditory meatus, bringing it out posteriorly through the opening in the posterior wall of the canal. Forcible traction on this strip of gauze will pull the obstructing tissues entirely beyond the field

[1] Medico-Chirurgical Transactions, vol. lxxxiii.

of vision and allow a perfect inspection of the parts lying at the fundus of the meatus. The operator may next proceed in one of two ways: he may either enter the mastoid antrum in the typical manner advocated by Schwartze in the performance of an ordinary mastoid operation, or he may proceed, as Stacke advises,[1] by first removing through the external auditory meatus the floor of the tympanic vault. I must confess that experience has taught me to recommend most strenuously entering the mastoid antrum through the cortex as the primary step. When performed upon the cadaver, where there is no hemorrhage, it is perfectly simple to introduce a chisel into the external auditory meatus and to remove the floor of the tympanic vault and a portion of the posterior wall of the canal. Where, however, the field of operation is more or less obscured by hemorrhage—and by this I do not mean the hemorrhage that can be controlled by clamping the principal bleeding points, but that oozing from the entire incised surface, which so frequently follows any surgical interference in this region—the landmarks are so obscured that in quite a large proportion of cases the chisel, if introduced into the external auditory canal, must be used somewhat blindly. In these cases I believe it is always wise to begin by perforating the cortex at the region of election and enter the antrum in this way. After the antrum has once been entered a probe will pass directly forward, downward, and inward into the tympanic vault. The next step is the breaking down of the posterior and upper wall of the external auditory canal, thus making the canal-like passage through the cortex into the mastoid antrum continuous with the external auditory canal and the middle ear. Certain important structures may be damaged in performing this step of the operation. In order to avoid wounding important structures the operator should proceed as follows: The antrum having been opened in the typical manner, the operator should proceed to follow the upper wall of the external auditory meatus down to the middle ear. If the bony tissues could be divided along this line no damage would be done to any important structures. In order to effect this division a certain amount of bone must be removed from below; consequently the operator should enlarge the opening through the mastoid cortex until it assumes a funnel-shaped form, the apex of the funnel lying at the mastoid antrum and the broad base of the funnel including an area of mastoid cortex and the external auditory canal, the vertical diameter of which is equal to that of the vertical diameter of the external auditory canal. In breaking down the wall between the canal and this funnel-shaped opening in the mastoid the operator should remove a wedge-shaped piece of bone, the base of the wedge corresponding to the vertical diameter of the meatus and the

[1] Loc. cit.

apex corresponding to the *aditus ad antrum*—that channel which joins the mastoid antrum with the tympanic vault. The important structures to be avoided lie just below the apex of this wedge-shaped piece of bone to be removed; they are the horizontal semicircular canal, which forms really the floor of the *aditus ad antrum*, and immediately below this the aqueductus Fallopii, which contains the trunk of the facial nerve; lower still we have the oval window, containing the stapes. If the operator proceeds from without inward he may follow the upper wall of the external auditory canal inward until the antrum is reached. He may follow the inferior wall inward for at least two-thirds of its length. The removal of the long bony partition along these lines will then reveal the prominence of the horizontal semicircular canal, and, immediately below this, that of the aqueductus Fallopii. If the posterior wall of the meatus is removed throughout its entire length as far as the internal wall of the middle ear, the horizontal semicircular canal and aqueductus Fallopii must be injured. The point which the operator should remember is to follow inward along the level of the inferior wall of the canal for about two-thirds of the length of the auditory meatus, while the bony tissue can be removed along the upper wall until the *aditus ad antrum* is reached. When this triangular, or really this quadrilateral, piece of bone has been removed the surgeon will be able to see distinctly the prominence of the horizontal semicircular canal and the facial nerve, and close inspection will reveal below this the oval window. After these steps of the operation have been accomplished the operator will then break away the floor of the tympanic vault—that is, the inner extremity of the superior wall of the external auditory meatus. This procedure, when completed, will disclose the entire middle-ear cavity as continuous with the external auditory canal. The head and neck of the malleus, with the short and long process, will be readily seen, the body of the incus, with its short process, resting in the cella incudis, and its long process extending downward; the incudostapedial articulation will likewise be made out. Above the head of the stapes the operator will see the prominent ridge which marks the horizontal semicircular canal, and immediately below, or more frequently amalgamated with it, the ridge of the aqueductus Fallopii, containing the facial nerve. It is then simple, after the parts are so thoroughly exposed, to divide the incudostapedial articulation, if it is still intact, and to remove the malleus and incus as well as any remnants of the drum membrane. All this can be done, in favorable cases, without disturbing the stapes. After the ossicles have been removed the entire cavity exposed should be thoroughly curetted until firm bone is encountered in every direction. In cases where the mastoid is pneumatic the large mastoid cells must be opened up, and these must be explored until firm bone is reached, and until the entire

bony cavity presents smooth walls in every direction. In cases where this operation is applicable we most frequently find the mastoid process sclerosed. The mastoid antrum is small, and most of the pneumatic spaces of the mastoid process are obliterated. In certain rare cases, however, we find the pneumatic cells very much diseased, and in every instance of this kind every vestige of pneumatic structure must be destroyed, so that the bony cavity remaining after the operation will present smooth and firm walls in every direction. (Fig. 1.)

While this procedure, if the operation could be performed as above described, would be exceedingly attractive, certain drawbacks not infrequently present themselves which render the operation difficult. In the first place, hemorrhage is one of the great hindrances to this operation, as it is to the simpler operation of ossiculectomy, already

FIG. 1.

FIG. 2.

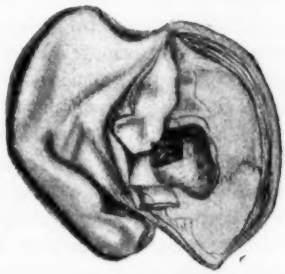

Fig. 1 is a complete Stacke-Schwartze operation. The mastoid cells and middle ear have been thrown into one large cavity continuous with the external auditory meatus. Dench Diseases of the Ear, third edition. (From dissections by the author.)

Fig. 2 is a Stacke-Schwartze operation. Formation of flaps by Panse method. Dench, Diseases of the Ear, third edition. (From dissections by the author.)

detailed in the early part of this paper. In the large majority of cases hemorrhage does not interfere seriously with the conduct of the operation, although it frequently prolongs the procedure unduly. I encountered one case—among those reported—where the general oozing was so profuse as to make the operation very long and tedious. The only way to control the hemorrhage is by packing the wound firmly with sterile gauze. In cases where the venous oozing is troublesome the operator must simply content himself with prolonging his operation until the hemorrhage ceases.

After all carious bone has been removed and the hemorrhage stopped from all bleeding points, the operator next proceeds to line the cavity with epithelial flaps derived from the posterior wall of the fibrocartilaginous meatus and from the concha. Several methods are much in

vogue in forming these flaps. Stacke, in his earlier operation, advocated the splitting of the fibrocartilaginous meatus along the posterior aspect and tucking the two triangular flaps thus formed, the one upward and backward and the other downward and backward, into the bony cavity formed by the enlargement of the fundus of the canal.

Panse modifies this procedure, converting the horizontal incision along the posterior wall of the canal into a T-shaped incision, by making one cut upward and another downward where the horizontal incision along the posterior wall of the meatus extends to the concha. In this manner two quadrilateral flaps are formed—one, which is turned upward, and the other downward, so as to more perfectly line the cavity formed by the extensive removal of the bone. (Fig. 2.) These two flaps are held in position by means of sutures which pass through the flaps and bend the upper flap forward and upward upon itself, while the lower flap is bent backward and downward upon itself. All sutures pass through the quadrilateral flaps and through the soft structures in the anterior flap.

FIG. 3.

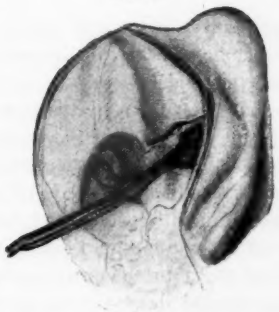

Fig. 3 is a Stacke-Schwartze operation. The long tongue-shaped flap, formed according to the Körner method, is seen drawn outward and backward by means of a clamp. Dench, Diseases of the Ear, third edition. (From dissections by the author.)

Another modification of the plastic operation is that of Körner, who, instead of dividing the fibrocartilaginous meatus by a single horizontal incision, makes one horizontal incision along the upper and posterior margin of the fibrocartilaginous tube, and the other along the posteroinferior margin. This incision is extended into the concha. In this way a single quadrilateral flap is formed which can be forced backward into the bony cavity. (Fig. 3.)

The cartilaginous structure of the concha interferes materially with the reflection of this flap backward into the bony cavity which it is supposed to line. In order to obviate this difficulty, Jansen, of Berlin,

advocated the dissecting out of the cartilage, thus making the flap thin and allowing of its easy displacement into the bony cavity.[1] I have attempted this method in one case, and the result was fairly successful.

Still another method is that recommended by Ballance,[2] in which a tongue-shaped flap is formed which includes practically the entire area of the concha. This flap is cut from the auricle by passing a thin knife into the external auditory meatus just behind the tragus. The knife is then passed downward and made to divide the integument along the entire anterior, inferior, and posterior aspects of the concha, the incision stopping just below the anterior crus of the antihelix. The tongue-shaped flap thus formed is dissected up from the underlying cartilage, and the cartilage is excised. This tongue-shaped flap is then turned upward and backward, and is held in position by retention sutures against the corresponding raw surface of the anterior auricular flap—that is, the two raw auricular surfaces are brought together. It will be seen that in this way a cutaneous flap is formed which, on turning the auricle backward, fits for a considerable distance into the upper and posterior portion of the bony cavity, and thus serves to line this with integument.

Ballance also advocates the subsequent lining of the entire bony cavity, at a period of ten days after the primary operation, with skin grafts after the Thiersch method.

From my own experience I can say I have formed flaps in all of the above-mentioned ways, and believe that the exact flap to be formed must depend upon the particular conformation of the parts in each individual case. I might say, in regard to the Panse method, that for some time I have adopted a modification which has been very valuable to me. Instead of bending the upper and lower flaps backward upon themselves and suturing them to the anterior flap, to which they are already attached, I have passed deep sutures through the entire depth of these flaps and sutured them to the periosteal margin behind the mastoid wound. These sutures have been buried, and have served to hold not only the flaps in place and to force them, respectively, well upward and downward into the canal, but have also served to bring the cutaneous margins of the external wound in pretty close apposition. I have then closed my cutaneous wound with interrupted silk sutures, or, in some cases, with catgut or silkworm-gut sutures, and the results have been very favorable. In a number of cases, for the last year, I have dissected out more or less of the cartilage of the concha, and in every instance have found the results of the plastic operation were much better when this was done than when the flaps were allowed

[1] Verhandlungen der Deutschen Otologischen Gesellschafte Siebenten Versammlung in Würzburg, p. 196.

[2] Loc. cit.

to remain in their original thickness. I have also made use of the tongue-shaped flap, with the dissecting out of the cartilage after the Ballance method, but have slightly modified the manner of holding the flap in position. I have never attempted to line the middle-ear cavity by means of the Thiersch grafts, by reopening the posterior wound, as advocated by Ballance, but in one instance secured an admirable result by lining the entire wound through the external auditory meatus, the opening which was left after the plastic operation being so ample that the grafts could be inserted without great difficulty.

As before stated, I do not believe that any one method of forming the flaps or of securing them in position is applicable to every case. The operator should bear in mind the different methods which can be employed, and should modify these in such a way as will best conserve the purposes of the operation in any individual case.

Certain accidents may occur during the course of the radical operation. These are injury to the facial nerve, injury to the horizontal semicircular canal, injury to the labyrinth, exposure or perforation of the dura in the middle cranial fossa, exposure or wounding of the lateral sinus.

The facial nerve is most frequently injured in curetting the middle ear. If the rule given in the early part of this paper—as to the procedure to be adopted for removing the posterior wall of the canal until the horizontal semicircular canal is seen—be uniformly followed, and if curettement of the atrium is delayed until the operator has made sure that he sees the semicircular canal, it will be almost impossible for either the facial nerve or the horizontal semicircular canal to be injured. Where this accident has happened in my own cases—and it has occurred in several—the fault has always been that I have been too cautious in removing the outer portion of the posterior canal wall. If the posterior wall of the bony meatus is removed carefully no damage can be done, as the hard, dense covering of the horizontal semicircular canal and of the facial nerve will be seen before they can be injured. When seen they are easily recognized and avoided. After these structures have been exposed great care should be exercised in curetting the tympanum, and the edge of the curette should be invariably directed upward, forward, and downward, but never upward, backward, and outward. A backward stroke of the curette may open the facial canal and injure the nerve.

The labyrinth may be injured either by forcible curettage of the internal tympanic wall, in cases where there has been extensive caries in this region, or this portion of the perceptive apparatus may suffer violence by the entrance of instruments through the oval window, or, in rare instances, through the membrane of the round window. It is a well-known fact that in most cases of intratympanic caries the foot-plate

of the stapes seldom suffers. The crura of the ossicle may disintegrate as the result of the intratympanic caries; but the foot-plate, owing to the fact that it receives its blood-supply both from its tympanic and labyrinthine surface, is seldom cast off. The injudicious use of the curette in the neighborhood of the oval window may injure the labyrinth either by crowding the ossicle inward and actually dislocating it into the labyrinthine chamber, or, in cases where the crura have been destroyed, a small curette may really destroy the foot-plate of the stapes and enter the vestibule. While in certain instances such an injury may be unavoidable, the operator should always bear in mind that the curette is to be used with extreme caution in this region. Too much force should not be employed, either, over the promontory, or particularly should not be used in the neighborhood of the oval window. The results following the incautious use of instruments in this region may result not only in an impairment of the hearing, but also in an infection of the labyrinth, which, spreading to the meninges, may lead to a fatal termination.

The exposure of the dura mater, in the middle cranial fossa, is not to be regarded as of any consequence. It is frequently necessary to expose the dura in this region, in order to remove all carious bone. In certain cases, where the internal table is perfectly normal, the operator will find it practically impossible to expose the tympanic vault and the *aditus ad antrum* without removing the thin lamella of bone which separates these spaces from the middle cranial fossa. Under strict aseptic precautions there is practically no danger of infection of the meninges if the dura is exposed. If the dura be accidentally perforated, thus exposing pia mater and brain substance to infection, the accident is certainly one of considerable gravity. In one case upon which I operated the middle cranial fossa was exceedingly low, and in removing the external wall of the vault by means of the chisel the internal table was involved in the section as well. A thin spicule of bone perforated the dura, and upon cautiously probing the wound I found that the probe entered through the dural perforation and penetrated the brain substance. As the case was one of purulent otorrhœa of long standing, I was naturally much disturbed, but proceeded with the operation, exposing freely the dura, and assuring myself that the perforation through this membrane was very small, and that no serious injury had been done to the brain substance. The operation was then carried out in the ordinary manner, great care being taken to remove every vestige of diseased bone, so that no secondary infection of the brain could result from the middle-ear suppuration. The operation wound was then drained entirely through the canal by means of gauze packing, and the line of incision was completely closed by means of sutures. This patient made a perfect and rapid recovery.

Injuries to the lateral sinus in cases where the radical operation is performed are extremely rare. Not infrequently, however, when the sinus lies far forward this vessel will be exposed during the operation. This has happened to me in several of my cases, but I have never seen any unfavorable results from this exposure.

It is much wiser to do a thorough and complete operation in these cases, exposing the dura in the middle cranial fossa or the lateral sinus in the posterior portion of the wound, rather than do a less complete operation in order to avoid the exposure of these structures. Accidental wounding of the lateral sinus will, of course, occasionally occur; and while the wounding of the vessel is more grave than its simple exposure, it need not necessarily be followed by any serious results. A firm tampon of iodoform gauze will invariably control the hemorrhage, and if the operation has been conducted aseptically there is very little danger of infection of the sinus.

In any operation conducted according to aseptic principles the occurrence of any of these accidents need not deter the operator from closing the posterior wound throughout and trusting to drainage through the external auditory meatus.

It is always wise to pack off either the area of dural exposure or any wound of the lateral sinus with a separate strip of gauze, to guard against subsequent infection through the packing which is introduced deep into the tympanic cavity at the site of original infection. It is always wise in these cases to change the dressing at the end of at least forty-eight hours after the operation, and then to dress the case every twenty-four or forty-eight hours until the wounded areas are completely protected by a firm layer of granulations.

I have gone into this subject rather fully, because I have desired to bring before you the advantages which accrue from each operation having for its purpose the removal of diseased bone from the middle ear. Both from the statistics of others and from my own statistics we may conclude that the simpler operation of ossiculectomy has a permanent place in the surgery of the middle ear.

In those cases reported by Panse[1] we find, as the result of the radical operation, 54 per cent. of cures, while Grunert[2] reports 52 per cent. In my own cases the reports show 72 per cent. of cures. Referring again to the statistics of the simpler operation, it will be remembered that of Grunert's cases, 46 per cent. were cured; in Ludwig's cases 51 per cent., in Schroeder's cases 48 per cent., while in the author's cases 57 per cent. were cured. It will be seen, therefore, that with few exceptions the percentage of cures is not so much greater for the radical operation than it is for the more simple procedure. I can easily

[1] Loc. cit.

[2] Loc. cit.

explain the apparent discrepancy in the ratio of cures in my own cases from the fact that in my earlier operations I was more inclined to perform the simpler operation of ossiculectomy, and therefore probably operated on many cases by this method which should more properly have been operated upon by the radical procedure. Of late years I have operated upon many cases by the radical method which might possibly have been cured by simple ossiculectomy. These cases would naturally recover perfectly after the radical operation. For this reason the percentage of favorable results following the radical operation is considerably higher than that of favorable results following ossiculectomy, and is also considerably higher than reported by other operators. I believe that the value of each procedure will depend upon the individual case. Where caries is limited, and where there is no history of recurrent attacks of acute inflammation of the middle ear, with marked symptoms of imperfect drainage, the simpler procedure is the one to be resorted to. On the other hand, where we have a history of recurrent attacks of acute inflammation of the middle ear in a case of purulent otitis media, and where, also, these acute attacks are accompanied by a train of symptoms which make one suspect that there may be beginning infection of the mastoid, of the labyrinth, or possibly of the intracranial structures, these cases should be invariably subjected to the radical operation.

One point which has not been mentioned in discussing these various operations is the effect which each procedure has upon the function of audition. In the more severe cases of purulent otitis media the hearing is often so poor that the operator may exclude entirely the possible effect of any operative procedure upon audition, and may feel that the only problem to deal with is the cure of the suppuration. In a certain proportion of cases, however, where the evidences of septic absorption are not very pronounced, and where the hearing in the affected ear is fairly good, the surgeon must bear in mind the possible effect of any operative procedure upon the function of that organ.

While I cannot give the exact percentages in my own cases, as many of the records have not been kept accurately, I will say that in my experience the result of an ossiculectomy has seldom been to reduce the hearing, but has in many cases materially improved the power of audition. Conducted carefully, the surgeon can practically promise the patient that, barring accidents, the hearing, after the removal of the ossicles, will be no worse than it was before, and will probably be somewhat improved. This statement applies to cases in which functional examination shows that the labyrinth has not been involved secondarily. In cases where secondary labyrinthine involvement has occurred the effect of ossiculectomy is not infrequently to cause an additional impairment of audition.

Referring to the work of others, I find that out of 130 cases of ossiculectomy reported by Schroeder, the hearing was improved in 65 per cent., in 22 per cent. it remained the same as before the operation, and in 13 per cent. it was impaired as the result of the operation.

Out of 43 cases reported by Ludwig the hearing remained the same after the operation as it was before in 19 cases, it was improved in 17, it was made worse in 3, the result was unknown in 2, while in 2 other cases the patients died.

Regarding the results of the radical operation, Grunert[1] says that in the greater proportion of cases the hearing remains the same after operation as before, while in certain cases it is considerably improved. My own experience with the radical operation leads me to believe that the surgeon is not warranted in promising the patient that the hearing will be as good after the operation as it was before unless at the time of operation the power of audition is very greatly dimininished in the affected ear. While during the course of the operation the surgeon may not injure any of the delicate structures within the tympanum, in those cases where the motility of the stapes approaches anything like the normal standard a certain rigidity of this ossicle must necessarily take place as the result of the epidermization of the tympanic cavity. The surgeon, therefore, should always caution the patient, prior to the performance of the radical operation, that the function of audition upon the affected side may be very decidedly impaired after the operation. In cases where the audition is good the possible effect upon the hearing, other things being equal, will cause the surgeon to choose the simpler operation of ossiculectomy rather than the more radical procedure. It must always be remembered, however, that in most of these cases which come to us the question is not so much one of either the preservation or improvement of the function of the organ as the removal of a serious menace to life. Here, where the hearing in the opposite ear is good, the surgeon should not hesitate to advise the radical procedure, in spite of the fact that the function of the organ will be thereby materially interfered with.

THE ENTRANCE OF AIR INTO THE VEINS.

By H. A. Hare, M.D.,

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I have read with a good deal of interest a paper upon this subject contributed by Dr. Malcolm Goodridge, of New York, to The American Journal of the Medical Sciences for September, 1902. So far as

[1] Archiv für Ohrenheilkunde, vol. xxxv. p. 209.

I am aware, the most exhaustive experimental work which has been done in connection with this subject is that of Dr. Nicholas Senn, which was published in the *Transactions of the American Surgical Association* for 1885, and my own work, reported in the *Therapeutic Gazette* for 1889, page 606. Dr. Senn's experiments involved the use of different kinds of animals, but my own were confined almost entirely to dogs, and were made in ignorance of the very valuable research which had previously been carried out by Dr. Senn.

Having been taught as a student of medicine that the entrance of air into a vein, even in a minute amount, was followed by most disastrous results during surgical operations—having been warned that should such an occurrence take place while giving an hypodermic injection death might ensue—I was struck with the fact that when intravenous injections of various substances were given to some of the lower animals, and considerable quantities of air entered a vein, no appreciable results took place even if the jugular vein received the air. After these observations on my part had been confirmed by a large number of experiments in which the injection of air took place inadvertently, I carried out quite an exhaustive study in which I deliberately injected air into the jugular vein of dogs for the purpose of seeing how large quantities could be borne without producing death, and demonstrated the innocuousness of these injections to medical students of the University of Pennsylvania, where I was then teaching, to several of my colleagues, and finally before the Philadelphia County Medical Society, on that occasion injecting as much as sixty cubic centimetres of air into the jugular vein of a small dog that weighed about twelve pounds without the production of any symptoms whatever. I mention these preliminary facts, as they have some bearing upon the remarks which are to follow, which remarks, to a certain extent, take issue with those of Dr. Goodridge, both as to his quotations from Dr. Senn and from myself and as to the conclusions which he draws from his own experiments.

In the early part of Dr. Goodridge's paper he states that the researches of Dr. Senn and myself impress him with the fact that the personal equation of an investigator plays no insignificant part; for, "on the one hand, Hare, after experimenting with some seventy dogs, asserts that even large quantities of air do little harm; . . . on the other hand, Senn found that small quantities of air when injected into the jugular vein proved fatal in a large percentage of his dogs." As a matter of fact, this statement in regard to Senn's results is incorrect, as will be seen when page 72 of Dr. Senn's brochure on this subject is examined, where, in his remarks on his experiments, he states that a small amount of air in the right side of the heart in a healthy animal gives rise only to temporary symptoms referable to the heart's action

and the pulmonary circulation; and, again, when he states, a few lines below, "that the danger attending the insufflation of air into the veins is proportionate to the amount of air introduced as well as the capacity of the right ventricle to resist intracardiac pressure." It is interesting in this connection, although not directly in point at this time, to remark that Dr. Senn found it practically impossible in all his experiments to cause the entrance of air into a vein of the neck or into the longitudinal sinus unless he employed a syringe for the purpose of injecting it.

At the close of Goodridge's paper he concludes that the entrance of air into the veins even in small amounts is to be dreaded, as it results in death. Whether this conclusion is correct as it relates to man is doubtful. As is well known, there are a number of cases on record in which air embolism is supposed to have been responsible for death in the human being, although, as far as I know, the possibility of ordinary embolism having produced death in these cases has not been excluded. There are other cases of air embolism in man which were not disastrous.

The point is that Dr. Goodridge is not justified in making the assertion quoted, nor do his experiments justify him in the still more radical assertion that he believes the statement that large quantities of air may be introduced into the veins without unfavorable results to be "pernicious teaching, and not supported by fact." The results of my work and that of Senn seem to prove that air embolism in small amounts is not usually lethal, while Goodridge's own experiments support our earlier researches instead of controverting them.

When we come to examine the experiments upon which Dr. Goodridge has based his conclusions we find that a serious error has occurred as to the amounts of air which he has injected. Surely a wounded vein would not be apt to draw in very large quantities of air, even if the patient was struggling violently, and the experiments of Senn and myself certainly prove that small amounts of air introduced into the veins of animals practically never result fatally; while if any further proof of the fact that air may enter a vein without producing death is required, I may state that I have in my own experience seen a considerable quantity of air—amounting to as much as from two to three cubic centimetres—injected into the median basilic vein of two human beings without producing any symptoms whatever; while a third patient, who received a similar dose, shortly afterward had a decided rigor, which at the time was supposed to be due to the fact that the saline solution was unduly cold, and not to the air embolus which entered inadvertently. It is a noteworthy fact that in all Dr. Goodridge's experiments enormous quantities of air were injected into the veins, and, furthermore, that this injection was completed within a very few moments. Thus in one dog, weighing forty pounds, seventy-five cubic centimetres was injected into

the femoral vein, which would be equivalent to the injection of three hundred cubic centimetres in a man of one hundred and sixty pounds—an amount which could scarcely enter a wounded vein during an operation by any possibility unless it was deliberately forced into it. So, too, in his Experiment No. 10, notwithstanding the fact that seventy-five cubic centimetres was injected into a dog weighing thirty-four and one-half pounds, recovery took place, so that five days later the animal was recorded as being perfectly well, and on the sixth day was again subjected to an injection of seventy-five cubic centimetres, with the result that the dog "died." It is a noteworthy fact, however, that in Dr. Goodridge's report of this experiment he states that when the thorax was opened, after the supposed death of the dog, the auricles were spasmodically contracting, the right ventricle was distended with air, the heart was fibrillating, and that this continued for fifteen minutes. It would seem possible, therefore, that had the "autopsy" not been performed so soon, the dog might have survived even the second injection, since other dogs that did not come to immediate "autopsy" recovered. In his thirteenth experiment the animal received altogether two hundred cubic centimetres of air, in injections varying from fifty to seventy-five cubic centimetres each; and although the animal was apparently dead, it eventually recovered and was killed with chloroform. This animal received an amount of air in twenty-four minutes, which is equivalent, in a man weighing two hundred pounds, to a litre, or about one quart; while in Experiment 15, three hundred cubic centimetres given to a dog weighing less than forty pounds did not produce death, and it required a total of four hundred cubic centimetres to produce this result. The equivalent to this injection in a man of 160 pounds would be about three pints of air.

It is not necessary to quote further experiments which illustrate the fact that the doses of air which were employed by Dr. Goodridge were so massive that their effects cannot be compared with those which are produced by those minute quantities of air which might, perchance, be drawn into a vein. It is also a noteworthy point that not only did some of Dr. Goodridge's dogs survive these enormous injections, but in several instances he states that they recovered so rapidly that subsequent experiments were made upon the same animals. According to his own summary of his results, nine dogs recovered after aspiration of their hearts, while two others, which finally recovered, required large quantities of air—"two hundred and fifty to four hundred cubic centimetres"—to be injected forcibly before the pulse disappeared temporarily.

Dr. Goodridge also states that rapid injection of air is an important factor in producing bad results, and *that considerable quantities of air may be slowly injected without any serious effect.*

I do not doubt that such a quantity of air as eight hundred cubic centimetres, or nearly a quart, would produce a disastrous effect if it found entrance to the jugular vein of a man, and I do not deny that much smaller amounts may cause alarming symptoms, or even death. My claim is—and it is supported by the exhaustive experiments of Senn and myself, my personal experience with air embolism in man, and by Goodridge's own observations—that even a large air embolus is not as fatal as a small air embolus has been thought to be, and that the danger of the occurrence of air embolism is very slight. As was proved by Senn's researches, it is useless to conclude from massive injections in dogs that small ones in man are deadly.

Finally, it is not to be forgotten that in all probability different resistance to air embolism exists in different animals. Rabbits and monkeys are very susceptible, whereas dogs and goats are extraordinarily immune.

THE RELATION OF THE THYMUS GLAND TO MARASMUS.

By Wm. Royal Stokes, M.D.,
Professor of Pathology,

John Ruhräh, M.D.,
Clinical Professor of Pediatrics,

and

C. W. G. Rohrer, M.D.,
Demonstrator of Pathology.

(From the Pathological Laboratory of the College of Physicians and Surgeons, Baltimore.)

In 1877, Parrot described a condition of wasting in infants under the name of athrepsia. Since then this condition has been the subject of considerable investigation and thought. Many different names have been given to it, such as marasmus, simple atrophy, and atrophia primitiva infantum, etc.

The term inanition should be used only for those cases of acute starvation occurring in infants, with their rather characteristic symptoms and course.

There are two conditions in which we see atrophy in infants: The primary cases, where the cause is as yet unknown, and those following definite pathological conditions, or the secondary cases. The dividing line cannot at this time be definitely drawn. All cases occurring in the course of the easily recognized diseases may at once be placed in the group of secondary cases—those following tuberculosis, for example. Clinically, most cases are seen in infants who have had improper food and care. Some authors would place these in the list of secondary cases. Such authors would consider these from another standpoint and regard the process of nutrition as twofold—digestion

as the first step, and assimilation as the second. They would place under the head of primary atrophy only those where the second factor was at fault; or, in other words, those cases receiving proper care and a physiologically correct diet. This is, we think, a division practically useless; and for the present, until we have definite information, the cases should be divided, from a pathological basis, into those where there are lesions of definite diseases, and those where there are no special and constant lesions heretofore described except the wasting of the muscles and body fat.

The more important contributions to the pathology of the condition are as follows:

Baginsky thought that the disease was due to an atrophy of the mucous membrane of the intestine, and that it was owing to this condition that absorption was interfered with, and hence the atrophy. He estimated the amount of nitrogen ingested and that excreted, and found the nitrogen absorbed in these atrophic infants was about 50 per cent. below the normal. Similar anatomical studies were made by Soltau Fenwick, in London.

Since that time many investigators have disproved this anatomical statement. In the majority of cases the changes observed were due to the stretching of the intestinal wall by distention with intestinal gases, and also partly, in many cases, due to post-mortem change.

Bendix found that Baginsky's estimate concerning the nitrogen was exaggerated; and Heubner and Rubner, as the result of experiments carried out in a somewhat different manner, formulated the idea that there was sufficient food taken and absorbed, but that the trouble was due to the auto-intoxication from the decomposition of food in the intestinal tract. Czerny is of the same opinion, but holds that the intoxication is of an acid nature. The French writers regard the condition as an infection or intoxication due to a subacute or chronic infection of the intestinal tract. Marfan has more recently stated that the condition is due to a lack of or a lessened activity of the nutritive ferments; this in turn being due to intestinal infection.

Escherich and Marfan both claim that the reason that mother's milk is a better food for a child, and that breast-fed children more rarely get severe atrophies, is that there are more nutritive ferments in mother's milk than there are in cow's or goat's milk.

Our ideas concerning nutritive ferments are as yet too vague to be of great value.

We may safely assert, we think, that the trouble is not due to the amount of food ingested, nor to the amount absorbed from the intestinal tract, but that it is due to malassimilation of the food material in the body.

Herard, at a subsequent date, Friedleben, and recently Mettenheimer, have pointed out that the size and condition of the thymus gland was

an index to the state of the nutrition of the body. Of this there can be no doubt; the fact rests upon a firm basis of trustworthy observations. In the course of our autopsy experience in infants we observed this same fact independently, and have noted also changes which, as far as we have been able to ascertain, have never before been especially described in connection with infant atrophy.

The function of the thymus is as yet unknown. It has been the cause of considerable thought and investigation, the results of which may be briefly stated as follows:

Kölliker and Beard think that it is the parent source of the leucocytes; Chiari and Ziegler that it acts in place of the lymphatic system in intra-uterine life until it is replaced by other lymph-forming organs (pharyngeal and faucial tonsils) taking up its function. It is intimately connected with the lymphatic system, as it is enlarged in the general lymphatic enlargement of Hodgkin's disease and in leukæmia and Paltauf's status thymicus. It atrophies in atrophy of the lymphatics as in that following thyroidectomy.

It has also some relation with the spleen. Friedleben found that as the spleen got larger the thymus grew smaller. Schaffer found that when there were numerous nucleated red blood cells in the spleen there were few in the thymus, and *vice versa*.

The thymus may be the seat of changes in general diseases, such as tuberculosis and syphilis, and may be the seat of tumors of various kinds, and of abscesses. Hemorrhages are not of infrequent occurrence, especially in infants who have been asphyxiated.

It has been found to be hypertrophied in some, but not all cases of acromegaly (43 per cent.), gigantism, Graves' disease, chlorosis, epilepsy, and somewhat in infections, although authors differ on this point. In thymic asthma resulting in death in young infants it has been found very much hypertrophied, and also in the cases described by Paltauf and others under the name of Paltauf's status thymicus. In these cases, in young adults dying rather suddenly of œdema of the brain, there is found to be enlarged thymus, general hypertrophy of the lymphatic system, and hypoplasia of the vascular system, particularly of the aorta, and a chlorotic condition.

It is apt to persist where there is goitre.

It has been found atrophied in atrophic conditions and in rickets. In idiots Bourneville found that it was present in only 27 per cent. Katz found it present in every case in sixty-one autopsies on mentally sound children.

Friedleben extirpated the thymus in dogs, and found that there were changes in the blood, disturbances of the growth, particularly of the bone, nervous symptoms, and hyperidrosis; in other words, a condition resembling rickets.

Friedleben also noted the atrophy of the thymus gland in atrophic conditions. His wonderful monograph, published in 1858, contains the results of eight years' investigation on three hundred autopsies. It is one of the most valuable treatises ever published.

D'Abelous and Billard, and later Camia, removed the thymus in frogs, and found that there occurred a pigmentation of the skin of the back and œdema. The frogs died in about twenty days of a myasthenia gravis like the Erb-Goldflam syndrome.

Carbone extirpated the gland in rabbits, and found that there was no influence on the growth, and that there was apparently no blood-forming function.

In thymic asthma a portion of the gland has been removed a number of times. Siegel took off a part in a boy, aged two and a half years, who had suffered from laryngismus stridulus, and Koenig took out a portion from a child, aged two months, who had dyspnœa from the eighth day. Both recovered.

Perrucker took out the entire gland in a child, aged two and a half years, who had stridor from fifteen days after birth. He had aphonia and dyspnœa. He recovered, and eight months later was perfectly well and showed no symptoms from the loss of the gland.

The thymus gland has been used therapeutically in a number of conditions—in Graves' disease with questionable results, probably none. Blondel claims to have got good results in chlorosis. Mettenheimer used it in a large series of cases of rickets, and could not come to any conclusion except that it seemed to improve the nervous symptoms. Mendel, of Essen, claims good results in over a hundred cases. Mettenheimer got no result in cases of infantile myxœdema, but cured a case in an adult. It has been used without result in acromegaly. Mikulicz claims to have got good results in goitre.

In dogs fed on thymus Minkowski found a new substance in the urine, with the formula of $C_4N_4H_7O_3$.

Svehla found that it contained a substance that could be extracted with water, and when injected it produced an increase of the pulse-rate and a lowering of the blood pressure—results similar to those produced from the thyroid.

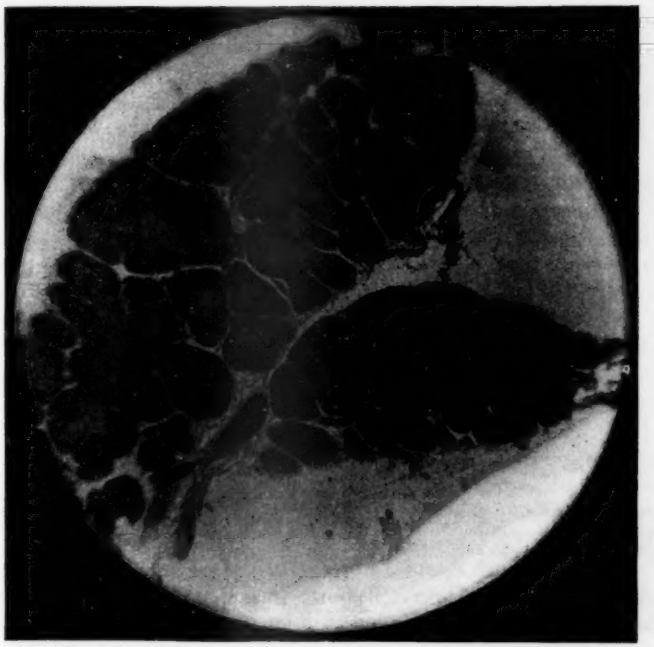
Bauman fed a dog on thymus, and found that the iodine in the thyroid was increased. He thinks that the two glands may have some antagonistic action.

Anatomy of the Thymus Gland. The thymus gland is a flat organ consisting of two lobes joined by an isthmus. These lobes are subdivided into many lobules separated by bands of fibrous tissue. It is situated in the anterior mediastinum, just above the pericardium and between the innominate and the left common carotid arteries. It is usually about 2 centimetres below the thyroid gland, and receives its

blood supply from the inferior thyroid artery. Its nerve supply is derived from the sympathetic system. In two cases of sudden death just after birth Mettenheimer found the glands weighing 12 grammes and 13.6 grammes, respectively. In young adults the average weight of the gland is about 22 grammes, and it generally measures 10 centimetres in length, 5 centimetres in breadth, and 1 centimetre in thickness.

EMBRYOLOGICAL DEVELOPMENT. The thymus develops in the embryo from the evagination of the entodermal epithelium of the third

FIG. 1.



Magnification same as Fig. 2. Normal thymus gland from a six months' fœtus, showing the contrast between the cortex and medulla of the lobules.

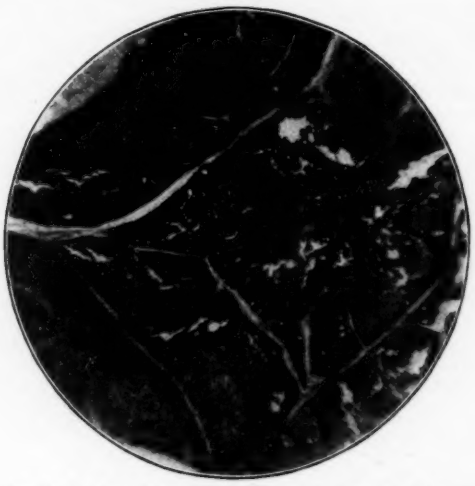
pouch of the gut tract. This layer of epithelial cells, by repeated branching, forms a structure similar to an acinous gland, which later becomes surrounded by mesodermic connective tissue and bloodvessels. Soon lymphoid cells make their appearance, when the gland assumes the structure found in extra-uterine life. The epithelial character thus soon becomes lost, and these cells only remain as the concentric masses known as Hassall's bodies, to be described later. The gland

assumes the structure of a lymphatic gland, and loses its previous epithelial character.

HISTOLOGICAL STRUCTURE. The thymus gland is surrounded by a loose fibrous capsule containing fibres of elastic tissue. This capsule penetrates between the lobules, forming trabeculæ, which serve as the framework of the structure, and stain by Van Gieson's connective-tissue stain.

The gland consists of a cortex and medulla, and the essential structure of the lobules of both cortex and medulla are similar. The lobule consists of a network of stellate endothelial cells with terminal

FIG. 2.



Projection ocular, No. 2, Zeiss; objective, a–2, Zeiss. Magnification, 23 diameters. Normal thymus gland from well-developed infant, showing sharp outline of cortex and medulla and normal trabeculæ separating lobules.

interlacing fibrils. These cells form the outer boundary of spaces which resemble the reticular spaces of lymphatic structures, and which contain many small lymphocytes. A few neutrophilic and eosinophilic leucocytes and giant cells are also found in these spaces. Here and there throughout the lobules there are islets of epithelium, and in the medulla of the gland the epithelial cells are arranged in a concentric manner, resembling in appearance the concentric bodies of an epithelioma. These are called the corpuscles of Hassall, or Hassall's bodies. They are the remains of the embryonic epithelial cells, which form the main portion of the gland during intra-uterine life.

During extra-uterine life these concentric bodies measure from 13μ to 175μ in diameter, and they usually consist of flat, concentric masses of

epithelium. The centre of these bodies often contains a number of shining, homogeneous granules, resembling hyalin. This material is produced by changes in the epithelial cells in the peripheral zone of the bodies. The most compressed, central cells first turn to keratohyalin, and are then transformed to true hyalin.

The gland is very rich in bloodvessels, and the adventitia of these vessels gradually becomes lost in the connective-tissue framework of the organ.

The arteries enter the central zone of the medulla of the thymus and break up into capillaries, which especially permeate the cortex. Those on the edge of the medulla break up into capillaries, which form anastomosing branches perpendicular to the surface. Immediately beneath the surface of the gland these capillaries spread out into a network of wide vessels, which join the venous radicles of the structure.

There is also a second system of veins which proceeds from the arteries in the medulla, and thus gives to the structure a double venous system.

The lymphatic system seems to begin in the lymph spaces scattered through the interlobular connective tissue. These gradually form lymph vessels, which assume a muscular coat, and soon show valves. These join the arteries which enter the gland, and convey the lymph from the organ.

Relationship between Infantile Atrophy and the Thymus Gland. Mettenheimer cites two cases of infantile atrophy in which the weights of the gland were 3.6 grammes and 2.1 grammes. The microscopic examination showed a great interlobular fibrous tissue increase, and the lobules had lost their normal lymphoid structure, the lymphocytes being supplanted by a proliferation of the endothelial cells resembling the precursors of connective-tissue increase. The concentric bodies were increased, and showed various stages of degeneration. Durante and Farret each found similar atrophic glands, weighing 1.5 grammes and 1.6 grammes, in a case of athrepsia or infantile atrophy.

The Pathological Changes in the Thymus Gland during Infantile Atrophy. Our investigations include the study of 18 cases of infantile atrophy or marasmus, in all of which cases autopsies were made.

The lowest weight of the thymus gland was 1.2 grammes (3 cases), and the highest weight was 7.5 grammes. The average weight in 16 cases was only 2.2 grammes. These present a great contrast to 2 cases with normal glands, in the table, which weighed 15 grammes and 19.5 grammes, respectively, and the general normal weight of 18 grammes.

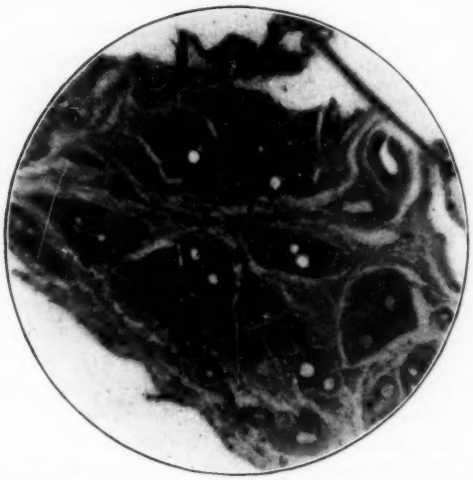
In all of the cases sections were studied from the heart, liver, kidney, spleen, lungs, stomach, and large and small intestines; and studies from some of the cases were made of the pancreas, adrenal gland,

thyroid gland, brain, various lymph glands, diaphragm, spinal cord, bladder, and aorta.

These specimens did not show any abnormal changes except occasional acute congestions or inflammations of the lungs due to terminal infection.

Cultures were made in 12 cases from the lung, heart, liver, kidney, and spleen, and they were all free from bacteria (an occasional infection excepted) except 4 cases. In 2 of these cases the lung contained pneumococci, and in the other case there was a streptothrix abscess of the lung present.

FIG. 3.



Magnification same as Fig. 2. Specimen of extreme atrophy from a case of severe marasmus (primary atrophy). This shows a great decrease in the number and size of the lobules, combined with great increase in the interlobular connective tissue. The hyaline degeneration of the Hassall bodies is well seen.

Excepting in the cases of terminal infection, the atrophy of the thymus gland was the only pathological process found, and the changes present in this gland will follow.

HISTOPATHOLOGY. The atrophied glands when examined under the microscope show conditions which differ widely from the normal. These changes also differ from those found in the normal involution of the gland.

The fibrous capsule of the gland is thicker than normal, and the trabeculæ are also greatly thickened, and the increased interlobular tissue frequently cuts up the lobules into irregular masses. This increase of connective tissue is often very apparent about the blood-

vessels, and even surrounds the dilated capillaries of the gland. Sometimes there is more fibrous tissue than lymphoid structure present in the field of the low-power lens.

In well-marked cases there is more reticular tissue present than normal, and the endothelial cells lining the reticular spaces are more numerous; consequently the lymphocytes and other cellular elements present in these spaces are decreased in number, and often the normal lymphoid structure of the gland is greatly altered.

This alteration of the lymphoid lobules at times entirely changes their appearance, and the changes can be described by reference to a description of one of the glands from a case of extreme atrophy:

"THYMUS GLAND. The capsule of the gland is greatly thickened, and the interlobular fibrous tissue proceeds from this area. The thickened bands between the lobules contain numerous veins and arteries, and the adventitia of these bloodvessels seems to thicken and produce an increase of connective tissue between the lobules, which is richly infiltrated with spindle-shaped or oval connective-tissue cells.

"All grades of atrophy can be made out in the lobules. Those least affected contain from five to fifty Hassall bodies containing many granular hyaline masses with leucocytes, often surrounded with an outer zone of more or less compressed epithelial cells. The lymphocytes are decreased in number, and the reticular endothelium is increased.

"The next stage seems to result in an almost entire disappearance of the lymphoid structure of the lobule and an increase in the reticular endothelium. These areas often contain many polymorphonuclear leucocytes and newly formed bloodvessels. This tissue greatly resembles fresh granulation tissue. This process continues until the lobule is transformed to a mass of capillaries separated by proliferated endothelial cells of various shapes and sizes. There are numerous loose spaces in the gland, separated by thin, fibrous walls, which almost resemble the air cells of the lung."

The state of nutrition of infants may be estimated by a microscopic examination of the thymus. In those of normal infants the structure of the thymus is unaltered, and the differentiation between cortex and medulla is plainly visible. In moderate atrophy the medulla and cortex are not easily distinguished, while in severe atrophies the changes described above are to be seen.

The connective tissue is often richly infiltrated with newly formed tissue cells, but no mast cells were seen on staining by polychrome methylene blue. Sometimes this tissue is infiltrated with fat cells.

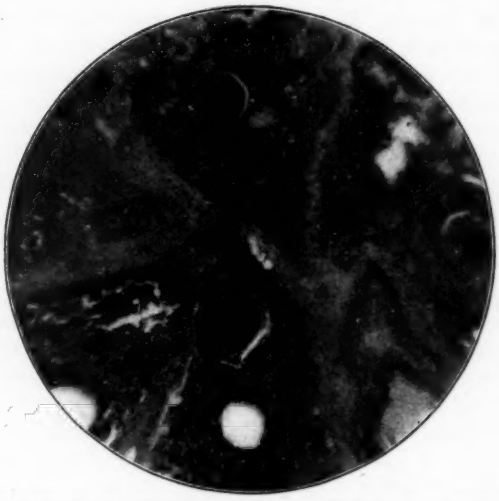
One of the most striking features present is the hyaline degeneration and increase in the size of the bodies of Hassall. These usually take up a bright rose-red stain by Van Gieson's method, although sometimes they stain an orange color.

We thought that these changes might be caused by a transformation of the epithelium of the bodies from keratohyalin into true hyalin, and in order to study this subject Dr. McCleary stained specimens from a number of cases of epithelioma of the skin.

When stained by Van Gieson's method the surface of the skin or horny layer stains a light yellow, and can be considered as true keratin.

The epithelial concentric bodies of the epithelioma which are regarded as keratohyalin stain an orange-yellow. A moderate number of these "pearls" contain globular masses which stain a rose-red color, and

FIG. 4.



Specimen same as Fig. 3. Magnification, 70 diameters. This shows enormous hyaline Hassall bodies stained by Van Gieson's method.

this is considered as the stain for true hyalin. As a distinction between true hyalin and colloid it was found that the colloid bodies of the prostate gland and the secretion of the thyroid gland give an orange color by Van Gieson's stain, and are therefore not true hyalin.

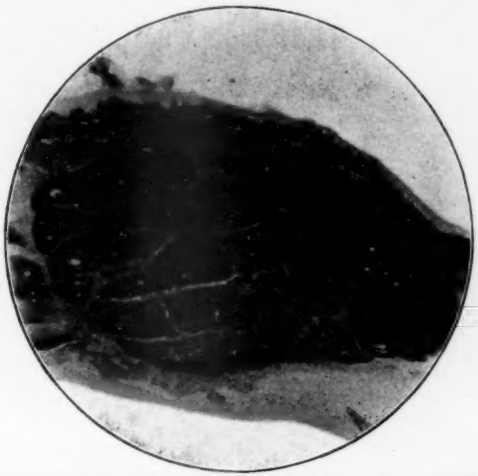
The study of the changes which take place in the Hassall bodies can be best done in atrophied glands, and the changes from epithelium to true hyalin were mainly observed in such specimens.

The thymus gland from fourteen case of infantile atrophy were stained by Van Gieson' method, and in one case the Hassall bodies stained orange, no true rose-red hyalin being present. This was from a case of only moderate severity. It can be stated as a general rule that the hyaline degeneration of Hassall's bodies is more marked in the glands showing the greatest atrophy.

In four cases the concentric bodies contained some material staining orange and some staining rose-red, showing the gradual transition from keratohyalin to true hyalin. These cases showed a moderate degree of glandular atrophy, and were taken from children in whom emaciation was only moderate in degree.

Nine cases showed a complete transformation into true hyalin, and in many of these glands the large rose-red masses measured from 200μ to 400μ in diameter. They at times appear as cysts, described by Chiari, and are always surrounded by a layer of flat epithelial cells. These degenerated structures are often infiltrated by polymorphonuclear leucocytes. These masses are sometimes homogeneous, and are sometimes made up of granules and compressed flat scales of various shapes and sizes.

FIG. 5.



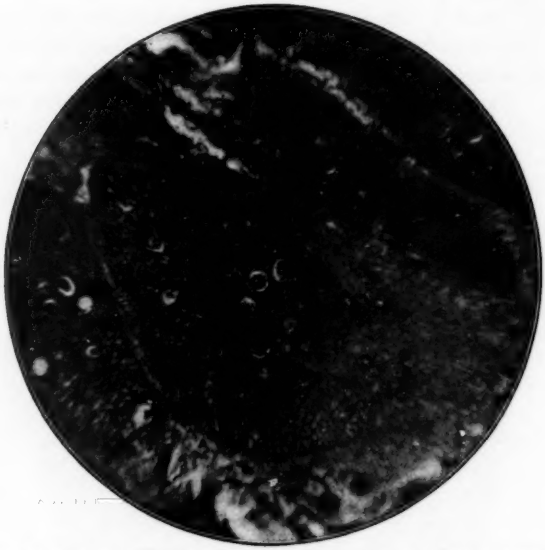
Magnification same as Fig. 2. Thymus gland, showing moderate atrophy from a case of secondary atrophy following tuberculosis. Differentiation of cortex and medulla absent. The increase of connective tissue most marked in the capsule. Hassall's bodies increased in number and size.

We paid special attention to the pathological changes in the stomach, duodenum, and small and large intestines. In a few cases we found certain areas in the mucous membrane and submucous coat which were completely necrotic, and sometimes the mucous membrane was missing from the surface. This often gives the appearance of great increase in the intertubular tissue, with only an occasional gland present separated by connective tissue.

If these changes were ante-mortem one should expect some inflammatory reaction or ulcer formation.

We did not find any such lesions, and are inclined to agree with the authors cited above in considering these nothing more than post-mortem changes. In many of our cases of marked infantile atrophy the mucous membrane of the intestinal tract was well preserved, and we do not associate such histological changes with infantile atrophy.

FIG. 6.



Same case of atrophy. Projection ocular, No. 2; objective, AA, Zeiss. Magnification, 70 diameters. This shows areas of increased fibrosis separating the lobules and many hyaline Hassall bodies.

SECONDARY ATROPHY OF THE THYMUS GLAND. By secondary atrophy of the thymus gland we wish to embrace those changes which take place in the organ during any of the chronic wasting diseases of children. Mettenheimer has shown in such diseases as tuberculosis, gastro-enteritis, rhachitis, and congenital syphilis that the thymus gland is decreased in weight. He made a number of microscopic examinations of the gland in these cases, and found fibrous increase, with marked hyaline degeneration of the Hassall bodies.

This author studied the thymus gland in 37 cases in children from three days to eleven years of age. From his examinations and tables he concluded that the weight of the thymus gland is the best index of the condition of the body nutrition.

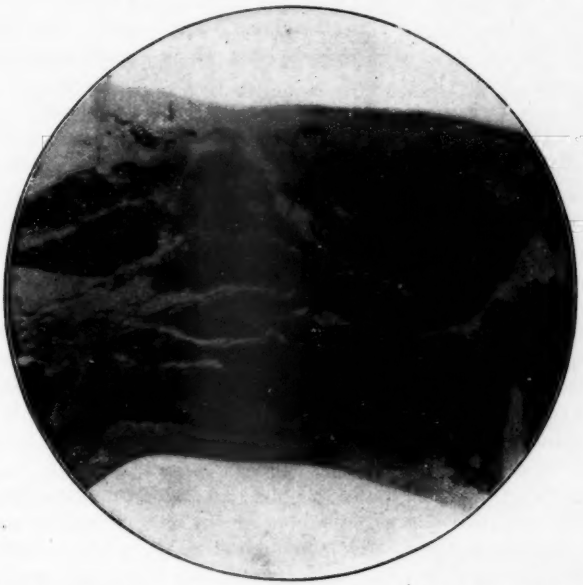
The normal weight of the thymus during the first two years of life, although subject to certain variations, seems to be about 18 grammes.

Mettenheimer found a certain reduction in weight during the acute diseases, but a much greater reduction occurred in the chronic wasting diseases.

The average weight in 7 cases of fatal diphtheria was 14.35 grammes, and in 11 cases of scarlet fever the weight was 12.05 grammes. These weights show a certain decrease as compared to the normal cases cited by various authors. The length and breadth of the gland were also diminished.

In 13 cases of such wasting diseases as miliary tuberculosis, congenital lues, and chronic enteritis the average weight was 4.5 grammes.

FIG. 7.



Magnification same as Fig. 2. Normal involution from adult, extensive fatty infiltration.

No special changes were found in the glands from the acute cases, but in the chronic diseases the following changes were noted:

The bloodvessels showed endarteritis, and the interlobular connective tissue was greatly increased. This caused an atrophy of the lobules and an obliteration of the lymphoid spaces by a proliferation of the endothelial cells. The lymphoid cells were decreased in number, and the gland had lost its normal structure. The Hassall bodies showed various stages of degeneration.

In two cases of tuberculosis of the lungs with general acute miliary tuberculosis, and in one case of tuberculous meningitis, we have been able to study the pathological changes in the thymus gland consequent upon the emaciation present.

We found that the difference was only one of degree between the changes in the gland of infantile atrophy and those of secondary atrophy. The thymus glands weighed, respectively, 3 grammes, 4 grammes, and 3.25 grammes, or an average of 3.41 grammes, the cases all being under one year of age. These weights show a marked contrast to the normal weight at birth of 12 grammes and 13 grammes given by Mettenheimer, and the normal of the first two years of life of 18 grammes.

All of these glands showed increased fibrosis, and hyaline degeneration and swelling of the Hassall bodies. In one case of tuberculosis these bodies contained calcareous deposits, which cleared up on adding 10 per cent. hydrochloric acid.

Although we have only studied a few cases of secondary atrophy, we can add those to the large number cited by Mettenheimer as a proof of the dictum that the weight of the thymus gland is the best index of the nutrition of the body.

Normal Adult Involution of the Thymus Gland. The thymus gland attains its greatest weight at the age of puberty, and from then on it undergoes a normal involution. The gland never entirely disappears, and traces of it can be found even in elderly persons.

The tissue undergoes a normal fatty infiltration, which begins first in the capsule, and gradually encroaches upon the cortex of the organ. The medulla resists this invasion longest, and persists as strips of lymphoid tissue with many hyaline Hassall bodies.

Sometimes the normal gland persists in adults and shows no retrogressive changes. Fig. 7 shows this condition well.

Clinical Observations. The fact that the thymus gland has been used with apparent success in the treatment of some cases of myxœdema might lead one to think that it would not be of value in a condition like infantile atrophy. The fact, however, that it has been used extensively in rhachitis without producing untoward results led us to a trial of it. With such marked changes in the gland it seems rational to think that it might be of value. Our cases have been too few to allow us to draw any conclusions.

In one set of cases the infants were under only fair hygienic conditions and the feeding not any too good. It was impossible to get the weights of the infants, and so the results were only to be measured by the eye. Twelve cases were given doses three times a day, starting with a grain and increasing until the dose had reached three grains of the dried gland. There was no appreciable change. Two of the infants

died—about what would have been expected without the treatment. After a month the treatment was discontinued. There was nothing of note in the condition of the children after the withdrawal of the drug. All of the other children are still living (two months later).

In another set the patients were admirably cared for, with the best of nursing, food, and surroundings. With the exception of the first case noted they were of the severe type of atrophy, and were not gaining under the best of conditions.

1. A very severe marasmus; died three days after admission. This case received six doses of thymus. The case was regarded as absolutely hopeless from the onset, and on admission was expected to die any minute.

2. *Severe Marasmus.* Age, three months; weight, 8¼ pounds; ½ grain t. i. d. After eight days had lost a quarter of a pound; dose increased to 3 grains; after a week had regained his original weight; three days later had a diarrhœa, apparently from intestinal indigestion. This persisted, and he lost ground, and finally died two weeks and a half later. At the time of death he weighed 6⅞ pounds. During the time of his intestinal disturbance he was also given subcutaneous injections of normal salt solution and other indicated treatment.

3. *Marasmus.* Age, two months; weight, 8⅜ pounds; thymus gland, 3 grains t. i. d.

Semiweekly weighings: 8⅜, 8⅜, 8½, 8¾, 8⅞, 9, 9¼, 9¼, 9¼, $8\frac{3}{4}^{x}$, 8½, 8½, 8½, 8½, and 8½ pounds. Died.

At the 8¾ weighing marked x the child had a temperature the cause of which could not be explained. It was transient, but the child never recovered from the effects of the hyperpyrexia.

4. *Marasmus.* Age, four months; weight, 8½ pounds; thymus gland, ½ grain; later, 1 grain t. i. d. Child gained steadily, and was discharged, cured, two months later, weighing 11 pounds.

Conclusions. 1. Atrophy of the thymus gland is always found in cases of infantile atrophy.

2. The condition of the thymus gland is an index of the general nutrition in infants.

3. The state of nutrition of infants may be estimated by a microscopic examination of the thymus at autopsy.

The authors are indebted to Dr. John S. Fulton for the photomicrographs in this article.

TABLE I.

No.	Anatomical diagnosis.	Weight of gland, grams.	Microscopic condition.	Other lesions.	Cultures.	Age.	Body weight.
1	Capillary bronchitis, atrophy of thymus.	1.4	Fibrosis, atrophy of lobules, hyalin degeneration of Hassall bodies.	Capillary bronchitis.	Pneumococci in lung.	3 mos.	5.1 lbs. 1.9 kilog.
2	Atrophy of thymus.	1.3	Fibrosis, few hyalin Hassall bodies.	Sections from 17 viscera normal.	Colon bacilli in lungs and liver.	14 dys.	2.75 lbs. 1.05 kilog.
3	Atrophy of thymus.	2	Interlobular and intralobular fibrosis; atrophy, hyalin degeneration.	Viscera normal.	Cultures 0.	7 wks.	5.5 lbs. 2.1 kilog.
4	Atrophy of thymus.	2.1	Interlobular fibrosis, hyalin degenerat'n.	Viscera normal.	Cultures 0.	15 dys.	4.62 lbs. 1.77 kilog.
5	Atrophy of thymus.	1.5	Interlobular fibrosis, hyalin degenerat n.	25 specimens of viscera normal.	.....	40 dys.	4.5 lbs. 1 5 kilog.
6	Abscess of left lung, atrophy of thymus.	2	Interlobular and intralobular fibrosis, marked atrophy of lobules, and hyalin degeneration.	Abscess of lung, red hepatization.	Streptothrix of lung,	18 dys.	4.0 lbs. 1.5 kilog.
7	Pneumonia of left lung, atrophy of thymus.	1.4	Same as above.	Purulent bronchopneumonia, other viscera normal.	Cultures 0.	3 mos.	6.0 lbs. 2.3 kilog.
8	Bronchopneum'nia, atrophy of thymus.	1.2	Interlobular fibrosis, hyalin degenerat'n, fatty infiltration.	Bronchopneumonia, other viscera normal.	Pneumococci in blood, aureus and pneumococci in lung and liver.		
9	Atrophy of thymus.	2	Interlobular fibrosis.	.....	Viscera sterile.	14 hrs.	6.0 lbs. 2 3 kilog.
10	Atrophy of thymus.	1.9	Interlobular fibrosis, atrophy, hyalin degeneration.	Viscera normal.	Streptococ. in lung by Weigert's method.	1 mo.	4.25 lbs. 1.6 kilog.
11	Bronchopneum'nia, serous pleurisy, atrophy of thymus gland.	3.2	Slight fibrosis and hyalin degenerat'n.	.....	.....	8 mos.	
12	Atrophy of thymus.	.....	Same as above.	.....	.....	18 mos.	
13	Atrophy of thymus.	4	Same as above.	Viscera congested otherwise normal.	.....	Premature.	3.5 lbs. 1.3 kilog.
14	Atrophy of thymus.	7.5	....	.....	.....	3 dys.	5.0 lbs. 1.9 kilog.
15	Atrophy of thymus.	1.2	Fibrosis and hyalin degeneration.	Viscera normal.	.....	5 wks.	4.75 lbs. 1.8 kilog.
16	Atrophy of thymus.	1.8	.....	Purulent bronchopneumonia, other viscera normal.	.....	1 mo.	5.5 lbs. 2.1 kilog.
17	Purulent bronchitis, atrophy of thymus.	.....	.....	Viscera normal.	.....	67 dys.	
18	Atrophy of thymus.	1.2	Interlobular and intralobular fibrosis, marked atrophy of lymphoid tissue, and hyalin degeneration.	Necrotic areas in mm. of small intestine, other viscera normal.	.....	2 mos.	

TABLE II.—NORMAL GLANDS FOUND AT AUTOPSY.

No.	Anatomical diagnosis.	Weight of gland, grams.	Microscopic condition.	Other lesions.	Cultures.	Age.
1	Congenital cyanosis.	15	Normal (see Fig. 2).	Thrombosis of left coronary artery, subdural hemorrhages; patent foramen ovale.	Negative.	14 hrs.
2	Meningocele, sudden death.	19 5	Normal.	.....	Blood and viscera sterile.	45 dys.

TABLE III.—SECONDARY ATROPHY OF THYMUS GLAND.

No.	Anatomical diagnosis.	Weight of gland.	Microscopic condition.	Other lesions.	Cultures.
1	Chronic pulmonary tuberculosis, acute miliary tuberculosis, tubercular meningitis.	3 grams.	Intralobular fibrosis, hyalin degeneration.	Tuberculosis of lungs, liver, spleen, and meninges.	Terminal infection with aureus.
2	Bronchopneumonia, retropharyngeal abscess, tubercular caries of spine, basilar meningitis.	(Atrophied.)	Marked interlobular and intralobular fibrosis, hyalin degeneration, atrophy of lymphoid tissue.	Bronchopneumonia, tuberculosis of the vertebræ, proliferative exudate in meninges.	Terminal streptococcus infection.
3	Chronic tuberculosis of lungs.	3.25 grams.			

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Below is found a partial list of references used in the preceding work. It has not been thought advisable at this time to publish the complete bibliography of the thymus gland.

Especial attention is called to the following: For a complete review and literature to 1858, see Friedleben; for historical facts and a comprehensive article, read Hennig; for modern ideas and list of references, see Mettenheimer and Klein.

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THE ANATOMY OF THE OPERATION OF REACHING THE ETHMOID CELLS THROUGH THE ANTRUM.

By Harris Peyton Mosher, M.D.,
assistant in anatomy, harvard university.

In working over some anatomical material I was struck with the ease with which the ethmoid cells—especially the middle and the posterior cells, which usually are so hard to get at—could be reached from the antrum through the upper part of its inner wall. Not only can these cells be opened up from here, but the sphenoidal sinus also. On the cadaver it is very satisfactory to see how directly and effectively this inaccessible region can be dealt with. It has been known for a considerable time that the antrum gives a good route to the sphenoid. In 1897, at the International Congress of Medicine at Moscow, Jansen reported a case of suppuration of the sphenoidal sinus which he had treated through the antrum. He found the ethmoid cells also diseased, and treated them likewise from the antrum. He was pleased with the method and advocated it. What I wish to do is to call attention to this route again, to consider briefly the applied anatomy of the operation, and to make it clear by means of diagrams.

If the antrum is opened from the canine fossa and the upper part of its inner wall along the line of the junction of the inner wall, and the roof of the antrum is examined, the following structures are found: The first quarter of an inch of the wall makes the outer boundary of

the lacrymal canal. The position of the canal is often indicated by a swelling. Just internal to this, or, if there is no swelling present, one-fourth to three-eighths of an inch from the surface, the ostium is placed. The ostium in some cases may be as much as one-half of an inch in; three-eighths of an inch, however, will usually clear the lacrymal canal. Beyond the ostium the upper part of the inner wall of the antrum is almost entirely membranous, except for the paper-like

FIG. 1.

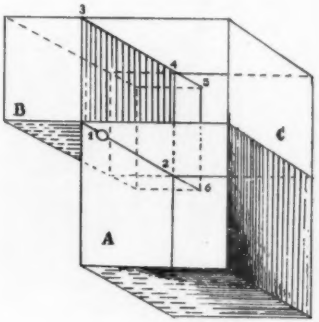

FIG. 2.

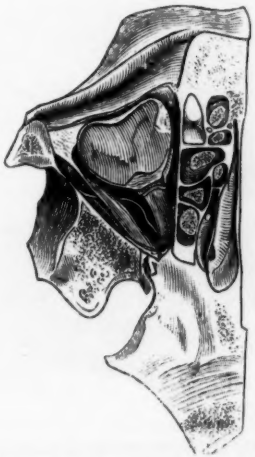

Fig. 1 shows in a diagrammatic way the relations of the orbit (C), the antrum (A), and the ethmoid cells (B). For the sake of clearness the sphenoidal sinus is represented as continuous with the ethmoid parallelogram. The figure shows particularly well the position of the ostium of the antrum (1) and the line of the incision for approaching the ethmoid region. The incision should start in the ostium and run directly backward about one-half of an inch, guided by the lower inner angle of the orbit. It would be represented by the line 1-2. In front of the ostium is the lacrymal duct. If the curette, therefore, is entered at the ostium, and not farther forward, the lacrymal duct is not in danger.

Fig. 2, a horizontal section through the orbit and the nose at the level of the cribriform plate—that is, the section is passed about one-eighth of an inch above the inner canthus of the eye. It shows the ethmoid parallelogram. The anterior boundary of this is the frontal bone, the posterior boundary the sphenoid; the outer boundary is the inner wall of the orbit, and the inner boundary the inner surface of the middle turbinal bone for the greater part, with just a little of the frontal. In a section made through the inner canthus of the eye (one-eighth of an inch below the section which is figured here) this sphenoid ceases to be a boundary.

process of the ethmoid (the uncinate), which projects downward and strengthens it. In 10 per cent. of the cases the antrum has a second ostium. This has no definite position. A knife, therefore, entered at the ostium, inclined toward the horizontal as much as the opening in the canine fossa permits, and carried directly backward, would cut only the membranous part of the wall, except, of course, this unimpor-

tant process of the ethmoid, and would bring up against the maxillary process of the palate bone. In many cases this is extremely thin, so that the knife would penetrate this and be stopped by the ascending process of the palate where it lies against the posterior inner angle of the superior maxilla, like one finger against another, and strengthens it. The lacrymal canal is entirely out of relation to the incision. The incision so made is about one-half of an inch long. No vessels of any size are cut. The inner wall of the antrum hangs like a curtain from the lower part of the inner angle of the orbit. The knife shaves it off

FIG. 3.

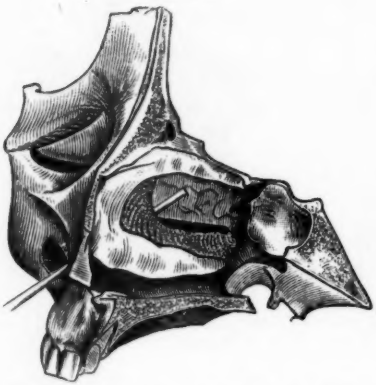

FIG. 4.

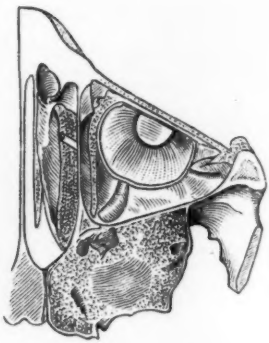

Fig. 3 shows the method of reaching the ethmoid cells from the antrum and the incision in the upper part of its inner wall through which this is accomplished. The anterior end of the incision is at the point where the probe is entered. (This corresponds to the ostium.) The crescentic line in front of this is the anterior border of the hiatus semilunaris. From the probe horizontally backward the heavy black line is the incision through which the cells have been reached Above this the drawing shows how the middle and posterior ethmoid cells have been cleared away, and farther back shows how the front wall of the sphenoidal sinus has been broken down.

Fig. 4 is the same region shown in Fig. 3, but from above. The ethmoid cells have been cleared away from below, as just described. The probe is pushed up into the empty ethmoid region through the ostium of the antrum. The inner wall of the middle turbinate hangs like a curtain on the inner side of the empty ethmoid space.

much as the mesentery is cut from the small bowel. For practical purposes the inner wall of the antrum can be regarded as made up much the same as it is in the disarticulated bone—that is, the first quarter of an inch is the outer boundary of the lacrymal canal; then comes the ostium, next one-half inch of membrane, and finally, for three-eighths of an inch, bone again.

A curette entered through the ostium, inclined toward the septum, and carried back in this incision would strike, first, the ethmoid bulla with the rest of the middle ethmoid cells, then the posterior cells, and,

finally, the anterior wall of the sphenoid. The ethmoid parallelogram is opened from its lower outer angle, and the cells can be removed by working upward and inward, toward the septum and away from the orbit. The height of the working space is the height of the os planum of the ethmoid minus the notch made in the upper wall of the ethmoid parallelogram by the dipping downward of the olfactory groove. This leaves the working space about one-half inch.

FIG. 5.

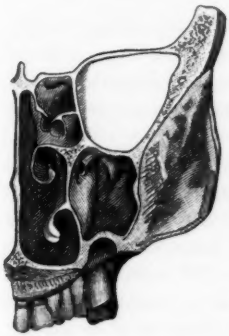

FIG. 6.

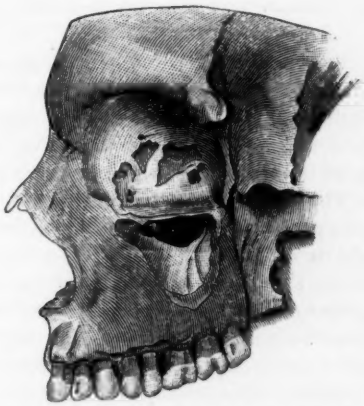

Fig. 5 is a horizontal section through the antrum, about one quarter of an inch behind the ostium. It shows the ethmoid parallelogram nicely, especially the lower outer angle, where it meets the orbit and the antrum. The anterior part of the inner wall of the antrum is also shown. The dark spot in the upper part of this is the ostium. In front of the ostium is the swelling made by the lacrymal duct. From this figure it is plain how an instrument entered at the ostium and pushed diagonally upward at once enters the ethmoid parallelogram.

Fig. 6 is copied from Watson Williams. It shows the inner wall of the antrum on the dried and cleaned skull. The dark area represents the membranous part of the inner wall. It is a little large in this specimen, because some of the paper-like uncinate process of the ethmoid has been broken off, as well as the maxillary process of the palate bone. It represents fairly, however, the area of the membranous wall from the operating standpoint.

In combined empyemata of the antrum and the middle and posterior ethmoid cells it would seem that this route should give good results. Where the frontal sinus is the sinus particularly affected I should doubt whether this method of dealing with the ethmoid region would be sufficient; but in those cases where the frontal suppuration is secondary to suppuration in the ethmoid region it might be of value.

TYPHOID FEVER IN CHILDREN OF TWO AND A HALF YEARS AND UNDER.[1]

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So much difference of opinion appears to exist regarding the frequency of the occurrence of typhoid fever in the first two years of life and the nature of the symptomatology, diagnosis, and prognosis at this time, that it has seemed to us possibly of use to study the subject a little more in detail than has hitherto been done.

The statements made in literature are much at variance and not always supported by facts or logic. The experience of one able pathologist is often quoted,[2] to the effect that in 2000 autopsies at the New York Foundling Asylum there was not found a single case with the lesions of typhoid fever. This would be as powerful evidence as negative evidence can ever be, were it not that the same writer[3] in another place makes the claim that the lesions of typhoid fever found at autopsy cannot be distinguished from those of enterocolitis. From this point of view the statements regarding the absence of typhoid lesions lose their value, for we have as good reason to assume that all the numerous instances of lesions supposed to be dependent on enterocolitis were really those of typhoid fever as to insist that they were the result of enterocolitis.

Another very able writer[4] is much quoted as having examined the blood of 50 children who might possibly be supposed to have typhoid fever, finding the serum reaction absent from all but one, an infant aged seven months, whose mother had had a slow fever ten years before. The conclusion appears to be that typhoid fever is rare. It would seem to us that the only conclusion allowable is that the writer possessed good diagnostic ability, since in none of the cases did he base a diagnosis upon clinical appearances. Besides, these observations are largely contradicted by those of Thursfield,[5] who found a typhoid reaction in 42 out of 100 sick children who presented symptoms which were at least more like typhoid fever than any other disease.

[1] Read before the American Pediatric Society, May, 1902.
[2] Northrup. Arch. of Pediat., 1895, vol. xii. p. 918.
[3] Ibid., 1896, vol. xiii. p. 16.
[4] Morse and Thayer. Boston Medical and Surgical Journal, 1899, vol. cxl. p 36.
[5] British Medical Journal, September 7, 1901, p. 596.

With statements, then, which are contradictory or self-destructive we are brought down to the question of mere facts, viz.: Do we find typhoid fever in infancy which by evident symptoms or by blood reaction is proved to be such, and if so how often does it happen? We have for years believed that the disease was of more frequent occurrence in early life than was commonly supposed, and the examination for the serum reaction but tends to confirm this. Not that typhoid fever is at all so common as later in childhood or in adult life. This *relative* infrequency is undisputed. But the statement that it is *actually* very rare under the age of two years certainly gives a wrong impression, and we are convinced that it does not correspond with the facts.

It is certain that the disease is repeatedly overlooked. Our experience has been very convincing in this regard, and is supported by that of many investigators, among whom may be mentioned Cassoute, J. L. Smith, Diem, Schavoir, Montmollin, Stowell and others. The failure to recognize it exists both because the possibility of typhoid fever being present is not thought of by the physician in charge, and because the difficulty of recognition is certainly greater in early life.

Any analysis of data regarding the individual cases which we have seen or have collected is necessarily somewhat unsatisfactory, because in some instances the histories are not complete, while in others no exact records of any sort have been kept. General deductions, rather than percentage figures, are the necessary consequent result.

The following case histories (Table I.) are given in brief. Some of the cases were under our own care; others occurred in the hospital service of colleagues, but were seen by us also; still others are kindly communicated to us by other colleagues. A few of them have been reported in a previous communication by one of us.[1] The others, we believe, have never been published.

TABLE I. PERSONAL AND UNPUBLISHED CASES.

Case 1 (reported in Philadelphia Medical Journal, October 15, 1898).—William H., aged three months, Children's Hospital; service of Dr. Griffith, February, 1897. Occasional vomiting for some weeks without diarrhœa; temperature not above 100°; frequent cough. Then rise of temperature, sometimes to 105°, with diarrhœa, debility, and stuporous condition; death without diagnosis. Duration about eight days from time of rise of temperature, probably longer. Post-mortem examination showed spleen and mesenteric glands enlarged; superficial ulceration of Peyer's patches; Widal reaction found in heart's blood.

Case 2 (reported in Philadelphia Medical Journal, October 15, 1898).—William G., aged seven months, Children's Hospital; service of Dr. Packard, June, 1895. Vomiting, diarrhœa, tympanites, and typical typhoid eruption; temperature, 103° to 105°; numerous furuncles also present; duration two weeks; death from exhaustion.

Case 3.—James D., aged one year, Children's Hospital, Out-patient Department; service of Dr. Packard, August, 1894. Diarrhœa for a week, with fever daily; examination showed abdomen swollen and tympanitic, typical typhoid eruption, mucous râles in chest; child appeared to have headache; lost sight of.

Case 4.—Louise S., aged fourteen months, seen in consultation with Dr. F. A. Baldwin, of New York, September 26, 1901. At thirteen months had milk poisoning, with enterocolitis

[1] Griffith. Philadelphia Medical Journal, October 15, 1898.

and fever; diarrhœa persisted for five weeks. Ten days before death, when apparently convalescing, there occurred a return of diarrhœa, with fever, tympanites, and typhoid eruption; later some spots became hemorrhagic; death ensued; duration five weeks, or ten days if dated from return of fever; no Widal reaction taken; diagnosis based upon eruption and general condition.

Case 5.—Joseph K., aged fifteen months, Children's Hospital; service of Dr. Packard, September 25, 1899. Three other members of the family had typhoid fever. Diarrhœa for a week; typical eruption and cough appeared, but no enlargement of spleen; temperature varied from 101° to 105° for two weeks, then became normal; Widal reaction positive; recovery; duration three weeks.

Case 6 (reported in Philadelphia Medical Journal, October 15, 1898).—Esther S., aged nineteen months, Children's Hospital; services of Drs. Packard and Griffith, October, 1897. Cough, anorexia, diarrhœa, enlarged spleen, eruption; temperature, 102° to 104°; Widal reaction positive; slight bronchopneumonia; recovery; duration about four weeks.

Case 7 (reported in Philadelphia Medical Journal, October 15, 1898).—Harry B., aged nineteen months, Children's Hospital; services of Drs. Packard and Griffith, October, 1897. Diarrhœa, anorexia, enlarged spleen, typhoid eruption, temperature, 100° to 102°; herpes; Widal reaction positive; recovery after complicating diphtheria.

Case 8 (reported by Dr. O'Malley, University Medical Magazine, 1897, vol. ix. p. 636).—Katie H., aged twenty-one months, St. Agnes' Hospital; service of Dr. Griffith, November, 1896. Diarrhœa, anorexia, tympanites, typhoid eruption; temperature up to 106.4°; duration twenty-three days; recovery. Father and mother and two other children ill in hospital with the disease at same time.

Case 9 (reported in Philadelphia Medical Journal, October 15, 1898).—Henry D., aged twenty-three months, seen in consultation with Dr. J. A. Patterson, of Salem, N. J., December, 1895. Vomiting, diarrhœa, cough, tympanites, dulness; temperature up to 104.8°; duration five or six weeks. Mother suffered with typhoid fever just before.

Case 10.—M. C., female, aged two years, St. Christopher's Hospital; service of Dr. E. W. Tully, December, 1895. Been ill one week; herpes, nausea, vomiting, tympanites, typhoid, eruption, diarrhœa; splenic tumor and cough developed; highest temperature, 103.6°; recovery.

Case 11.—Robert B., aged two years, seen in consultation with Dr. I. E. Roberts, March 26, 1899. Fever (104°) for two weeks; no diarrhœa or epistaxis; occasional vomiting and cough; typhoid spots and enlargement of spleen appeared; recovery.

Case 12.—Antonio G., aged two years. Children's Hospital; service of Dr. Stengel, August 26, 1901. Headache, abdominal pain, diarrhœa, tympanites, eruption, and fever (103.6°); lasting sixteen days in hospital; positive Widal reaction; recovery. Brother with typhoid fever.

Case 13.—Fannie B., aged two years and three months, Children's Hospital; service of Dr. Stengel, August, 1901. For a week abdominal pain, headache, and diarrhœa; had splenic tumor, tympanites, and eruption; fever (102.5°) became normal in two days after admission; Widal reaction positive. Scarlet fever then developed, and child was discharged on the 22d.

Case 14.—Marie S., aged two years and four months, seen in University Hospital; service of Dr. Tyson, December, 1897. Fever, diarrhœa, stuporous condition, enlarged spleen, no eruption, pneumonic consolidation; duration ten days. Post-mortem examination showed lesions of pneumonia, enlargement of spleen, Peyer's patches, and mesenteric glands; very slight evidence of ulceration. Mother and brother in hospital with disease.

Case 15.—Edward R., aged two years and five months, seen November, 1901, at close of illness. Had been fretful for two weeks; temperature about 105° for a week, nearly normal when first seen; disease had not been recognized by attending physician; Widal reaction positive; recovery.

Case 16.—Rosie M., aged two years and six months, Children's Hospital; service of Dr. Griffith, August, 1899. Ill six days with fever up to 105°; eruption and enlarged spleen; fever lasted seventeen days in hospital, when diphtheria developed; Widal reaction positive. Removed from hospital; result unknown.

Case 17.—Rachel G., aged two years and six months, Children's Hospital; service of Dr. Carpenter, August, 1899. Vomiting and constipation one day; fever ranging from 102° to 106° for a week; Widal reaction positive. Diphtheria then developed; tympanites, parotitis, otitis media, bronchopneumonia and submaxillary abscess followed; died four weeks from onset.

Case 18.—Evelina F., aged two years and six months, Children's Hospital; service of Dr. Packard, August, 1900. For two days diarrhœa, epistaxis, and fever up to 103°; tympanites splenic tumor, and typhoid eruption followed; temperature reached normal in eleven days; six days later recrudescence followed, lasting three days. Brother with typhoid fever.

From medical literature we have collected a number of cases reported as typhoid fever in which the data are given with sufficient detail to make the reports of some statistical value. Undoubtedly many cases have been overlooked. For convenience of reference we have given the principal data in a series of tables, and have included among the cases those of our own already given in Table I.

In all of the tables we have marked * those cases which have been reported as typhoid fever, concerning the diagnosis of which there may be some doubt, yet which appear to us as probable instances of the disease. Those marked **, although reported as typhoid fever, seem to us to be probably not properly so named. The word "eruption" always indicates typhoid roseola.

The first of the following tables (Table II.) includes cases in which there is reason to believe that the children were suffering from the disease when born.

TABLE II. CONGENITAL TYPHOID FEVER.

Case 1 (Freund and Levy, Berlin. klin. Wochenschr., 1895, xxxii. 539).—Male, aged six fœtal months at birth; mother in fourth week of typhoid; died when fifteen minutes old. At autopsy enlarged spleen and typhoid bacilli found (no intestinal lesions).

Case 2* (Manzini, Gaz. Méd. de Paris, 1841, ix. 781).—Aged seven fœtal months at birth; mother with typhoid; died when twenty minutes old. Peritonitis (?) at autopsy.

Case 3 (Legry, Thèse de Paris, 1890).—Aged seven fœtal months at birth; mother in fourth day of relapse; died when four days old in incubator; typhoid bacilli in liver.

Case 4 (H. C. Westervelt, Pennsylvania Medical Journal, 1902, v. 368).—Aged seven and a half fœtal months at birth; mother in third week of typhoid; fever (106°), diarrhœa, convulsions; duration seventeen days; recovery.

Case 5 (Chambrelent and St. Philippe, Journ. de Méd. de Bordeaux, 1896, xxvi. 502).—Aged eight fœtal months at birth; mother with typhoid; cough, enlarged liver, jaundice; Widal reaction positive.

Case 6* (F. W. Lynch, Journal American Medical Association, 1901, xxxvi. 1136).—Aged eight and a half fœtal months at birth; mother in fourth day of typhoid; eruption, symptoms of inanition; Widal reaction negative; died when seventy days old. At autopsy intestinal lesions and colon bacilli found.

Case 7 (Janiszewski, Münch. med. Wochenschr., 1893, 705).—Aged eight and a half fœtal months at birth; mother in tenth day of typhoid; bronchopneumonia; died when five days old. At autopsy typhoid bacilli in spleen, lungs, kidneys, and mesenteric glands (no intestinal lesions).

Case 8 (Paul Ernst, Ziegler's Beiträge zu path. Anat., 1890, viii. 188).—Almost at term; mother in eleventh day of typhoid; jaundice and eruption; died when ninety-three and a half hours old. At autopsy typhoid bacilli in spleen, muscles, spots, and blood.

Case 9 (M. A. Brown, Cincinnati Lancet-Clinic, 1901, N. S., xlvi. 387).—Almost at term; mother in eleventh day of typhoid; enlarged spleen, diarrhœa, fever; Widal reaction positive; died when fourteen days old. At autopsy enlarged spleen and mesenteric glands; typhoid bacilli.

Case 10** (Charcellay, Arch. Gén. de Méd., 1840, 3 s. ix. 65).—Male, at term; died when eight days old. At autopsy enlarged intestinal follicles, Peyer's patches, and mesenteric glands.

Case 11** (Ibid.).—Male, at term; diarrhœa, stomatitis; died when fifteen days old. Typical lesions at autopsy.

Case 12** (A. Bednar, Die Krank. der Neugeborenen und Säuglinge, 1850, i. 111).—Male, at term; eruption, fever, meteorism, vomiting, diarrhœa appearing on fifth day of life; duration eleven days; died when sixteen days old. Typical lesions at autopsy.

Case 13** (Ibid.).—Female, at term; diarrhœa, enlarged spleen; died when eleven days old. Typical lesions at autopsy.

Case 14** (Ibid.).—Male, at term; diarrhœa; died when fifteen days old. Typical lesions at autopsy.

Case 15** (Vibert, Ann. d'Hyg., 1881, vi. 3 s., 353).—Male, at term; died when nine days old. At autopsy enlarged spleen, mesenteric glands, and Peyer's patches.

Case 16* (W. Ignatieff, Medicinskoje Obosrenje, 1883, xx. 341).—Male, at term; mother supposed to have typhoid; fever, diarrhœa, and intestinal hemorrhages; died when nine days old. At autopsy enlarged spleen, ulcerated Peyer's patches and intestinal follicles, ecchymoses.

Case 17* (A. E. Okey, Peoria Medical Monthly, 1886-1887, vii. 419).—At term; mother with typhoid; fever, diarrhœa; died when ten days old.

Case 18* (W. W. Johnston, American Journal of Obstetrics, 1895, xxxi. 283).—At term; mother with typhoid and other cases in house, epidemic; fever, constipation, tympanites; died when five days old.

Case 19 (H. Dürk, Münch. med. Wochenschr., 1896, 842).—At term; mother in twenty-fourth day of typhoid; died in nine hours. At autopsy enlarged spleen, typhoid bacilli, and staphylococci found.

Case 20 (W. Osler [quoted by H. A. Hare, "Complications and Sequels of Typhoid Fever," 31]).—At term; mother with typhoid; died when five days old from perforation.

Case 21 (G. Blumer, Journal of the American Medical Association, 1900, xxxv. 1674).—Female, at term; mother had typhoid four and a half months before birth of child; convulsions, hemorrhages, and purpura; died when nine days old. At autopsy intestinal follicles, spleen, and all organs hemorrhagic; typhoid bacilli found.

Case 22 (J. Finley Bell, Arch. of Pediat., 1901, xviii. 348).—Female, at term; mother in fifth week of typhoid, other cases in house, epidemic; fever (103.6°), eruption, jaundice; Widal reaction positive; duration eight days; recovery.

Case 23 (J. M. Krim, Pediatrics, 1901, xii. 378).—Male, at term; mother in second week of typhoid; fever (103.5°); duration seventeen days; recovery.

Of these 23 cases reported as congenital typhoid fever, 12 may reasonably be considered genuine cases of the affection; 5 (marked*) are doubtful, yet are probably instances of the disease; 6 (marked**) are doubtful, and seem to us as probably not cases of typhoid fever, at least as far as the data given indicate; 8 patients were males, 3 females; in 12 the sex is not stated. In 17 cases the mothers had typhoid fever, and 2 cases occurred during house epidemics in which others in addition to the mothers were affected. Fever was noted in 6, diarrhœa in 8, constipation in 1, eruption in 3, enlarged spleen in 6, cough in 2, convulsions in 2, jaundice in 3, tympanites in 2, hemorrhage in 2, and vomiting in 1.

Recovery ensued in 3 cases, death in 19, and in 1 the result is not given. Typhoid bacilli were found in 6 of the 19 fatal cases. A positive Widal reaction is mentioned in 3 cases; a negative reaction is mentioned once.

We have considered in this group only children born *alive*, omitting from our list instances of purely *fœtal* typhoid, in which the evidence of the disease has been found in the fœtus or in the stillborn child. A number of cases of fœtal typhoid fever have been previously collected and published by one of us (Griffith, *Medical News*, May 15, 1897), and later added to by Morse (*Archives of Pediatrics*, 1900, xvii. 881).

In this connection may be mentioned the fact that newborn or very young infants, born of mothers suffering from typhoid fever, may exhibit the Widal reaction, yet without showing any other symptoms whatever of the disease. In such cases it is possible that the subjects have had typhoid fever *in utero*, or that the agglutinating principle may have

passed from the diseased mother into the healthy child through the placenta, or possibly later through the milk. The following cases (Table III.) may be mentioned as instances in point:

TABLE III. APPARENTLY HEALTHY INFANTS GIVING A POSITIVE WIDAL REACTION.

Case 1 (J. C. Wilson, Keating's Cyclopædia of the Diseases of Children, 1899, v. 168).—At term; mother in third week of typhoid; Widal reaction positive; recovery.

Case 2 (J. P. Crozer Griffith, Medical News, May 15, 1897).—At term; mother in third week of typhoid; jaundice; Widal reaction positive; recovery.

Case 3 (Mossé and Daunic, Compt. Rend. de la Soc. de Biol., 1897, 10 s., iv. 238).—At term; mother had recovered from typhoid one month before birth of child; Widal reaction positive; recovery.

Case 4 (Achard, Bull. et Mém. de la Soc. Méd. des Hôp. de Paris, 1899, xvi. 56).—At term; mother just recovered from typhoid; Widal reaction positive; recovery.

Case 5 (J. L. Morse, Arch. of Pediat., 1900, xvii. 898).—At term; mother in twelfth day of typhoid; Widal reaction positive; recovery.

Case 6 (J. L. Morse, Boston Medical and Surgical Journal, 1899, cxl. 86).—Aged seven months; mother had typhoid ten years before; diarrhœa; Widal reaction positive; recovery.

In the next table (Table IV.) are contained cases of typhoid fever up to but not including the age of one year, and excluding the instances of congenital typhoid fever already detailed. Although the first two may possibly have had the disease in the system before birth, yet, as there were no symptoms at birth, it is but right to include them among the cases of disease acquired later.

TABLE IV. TYPHOID FEVER IN THE FIRST YEAR.

Case 1 (A. Jacobi, Pediatrics, 1899, viii. 527).—Aged nine days; mother with typhoid; eruption, fever, diarrhœa, enlarged spleen; duration seven days; death. Autopsy: swollen Peyer's patches, enlarged spleen, no ulceration.

Case 2* (Hecker [quoted by Henoch, Vorlesung. ü. Kinderkr.]).—Female, aged thirteen days; in a room previously occupied by a typhoid case; fever, diarrhœa; duration three days; death. Autopsy: typically enlarged and ulcerated Peyer's patches.

Case 3 (Gerhardt, Handb. der Kinderkr., 1877, ii. 373).—Male, aged twenty-one days; born prematurely at eight months, on eighth day of mother's typhoid; not nursed, but kept in same room; fever (103.5°), diarrhœa, vomiting, eruption, enlarged spleen; duration four weeks; recovery.

Case 4 (A. Jacobi, Arch. of Pediat., 1892, ix. 763).—Aged three weeks.

Case 5 (Ibid.).—Aged six weeks.

Case 6** (Hauner, Beiträge zu Pediatrik., 1863, 45).—Aged two months; death. Autopsy: typical intestinal lesions.

Case 7** (Vibert, Annal. d'Hyg., 1881, 3 s. vi. 353).—Aged two months; previously healthy child; died suddenly. Autopsy: enlarged spleen, mesenteric glands, and Peyer's patches (no ulcers).

Case 8 (Hölscher, Münch. med. Wochenschr., 1891, 43).—Male, aged two months; mother with typhoid, nursing child.

Case 9 (Vouillemin, Thèse de Nancy, 1892, 12).—Male, aged two months; three other cases in the house; fever and eruption; duration four days; death. Autopsy: typical ulcers in small intestine.

Case 10 (Cassoute, Rev. Mens. des Mal. de l'Enf., 1898, xvi. 628).—Aged two months; epidemic, child bottle-fed; diarrhœa and collapse; Widal reaction positive; death. Autopsy: ulcerated Peyer's patches, congestion of the lungs.

Case 11 (C. C. Hubbard, Medical News, 1899, lxxv. 857).—Aged two and a half months; mother with typhoid, nursing child; fever, tympanites, diarrhœa, enlarged spleen; recovery.

Case 12** (Hennig [quoted by Gerhardt, Handb. d. Kinderkr., 1877, ii. 373]).—Aged three months; pneumonia; death. Autopsy: enlarged spleen, swollen Peyer's patches.

Case 13** (Wunderlich, Handb. der Path. und Ther., iv. 289).—Aged three months; eruption; death. Autopsy: typical lesions.

Case 14 (E. Rosenthal, Pediatrics, 1897, iv. 38).—Aged three months; mother with typhoid; recovery.

Case 15 (J. P. Crozer Griffith, Philadelphia Medical Journal, October 15, 1898). Case 1, Table I.—Male, aged three months; diarrhœa, fever, cough; Widal reaction positive after death; duration fourteen days; death. Autopsy: enlarged spleen and mesenteric glands, ulcerated Peyer's patches.

Case 16 (Legry, Thèse de Paris, 1890).—Aged four months; death. Autopsy: typhoid bacilli found.

Case 17 (H. N. Read, Brooklyn Medical Journal, 1889, iii. 599).—Female, aged four and a half months; epidemic; fever (105°), diarrhœa, tympanites, eruption; duration seventeen days; death.

Case 18 (J. G. Ogle, Lancet, 1892, i. 21).—Female, aged four and a half months; one of twins, on condensed milk; fever, vomiting; duration seven days; death. Autopsy: ulcerated Peyer's patches, enlarged mesenteric glands.

Case 19 (R. J. Love, British Medical Journal, 1902, i. 961).—Female, aged four and a half months; mother with typhoid, nursing child; fever (103°), enlarged spleen, diarrhœa, tympanites, cough, eruption; duration ten days; death.

Case 20** (Vibert, Annal. d'Hyg., 1881, vi. 353).—Male, aged five months; previously healthy child; sudden death. Autopsy: enlarged Peyer's patches and mesenteric glands (no ulcers).

Case 21 (C. W. Earle, Arch. of Pediat., 1892, ix. 734).—Male, aged five months; fever (103°), diarrhœa, tympanites, collapse; duration thirty days; death. Autopsy: typical lesions (no bacilli found).

Case 22 (W. S. Christopher, Arch. of Pediat., 1892, ix. 757).—Female, aged five months; fever, hemorrhage; recovery.

Case 23 (J. M. Taylor, Philadelphia Polyclinic, 1896, v. 286).—Aged five months; three other cases in house; fever, enlarged spleen, diarrhœa, tympanites; recovery.

Case 24 (S. Davidson, British Medical Journal, 1902, i. 1144).—Aged five months; diarrhœa, fever (102.4°), eruption; duration five weeks; recovery.

Case 25** (J. Abercrombie, Edinb. Med. and Surg. Rev., 1820, xvi. 334).—Aged six months; diarrhœa, vomiting, fever; duration six days; death. Autopsy: ulcerated Peyer's patches, enlarged mesenteric glands.

Case 26* (E. Friedrich, Der Abdominaltyphus der Kinder., 1858, 8).—Male, aged six months; epidemic; fever, diarrhœa, cough, convulsions; duration six days; death. Autopsy: enlarged spleen, mesenteric glands, and Peyer's patches.

Case 27* (Murchison, Transactions of the London Pathological Society, 1864, xvi. 125).—Female, aged six months; mother with typhoid, nursing child; eruption; death. Autopsy: ulcerated Peyer's patches and enlarged mesenteric glands.

Case 28* (E. Henoch, Charité-Annalen, 1875, ii. 510).—Female, aged six months; fever (104°), cough, diarrhœa, otitis, enlarged spleen; death. Autopsy: enlarged spleen.

Case 29* (A. Wiltshire, British Medical Journal, 1879, i. 427).—Male, aged six months; epidemic; fever, eruption, diarrhœa, relapse; recovery.

Case 30* (Ibid.).—Male, aged six months; epidemic; "clinically typical;" recovery.

Case 31** (Vibert, Ann. d'Hyg., 3 s., vi. 358).—Aged six months; previously healthy child; sudden death. Autopsy: typical lesions.

Case 32 (Parrot [quoted by Chantemesse, Traité des Mal. de l'Enf., i. 772]).—Aged six months.

Case 33 (M. P. Jacobi, Arch. of Med., 1884, xi. 30).—Aged six months: diarrhœa, fever, cough, tympanites, vomiting, eruption, enlarged spleen; duration three weeks; recovery.

Case 34 (E. Chenery, Journal of the American Medical Association, 1881, xvi 463) —Aged six months; mother with typhoid, nursing child; typical symptoms; duration three weeks; recovery.

Case 35 (H. J. Lee, Cleveland Journal of Medicine, 1897, ii. 400).—Aged six months; another case in house; fever (104.6°), diarrhœa, tympanites, cough, enlarged spleen; duration five weeks; recovery.

Case 36** (J. Abercrombie, Edinb. Med. and Surg. Rev., 1820, xvi. 334).—Aged seven months; after weaning; fever, vomiting, diarrhœa; duration five days; death. Autopsy: minute ulcers and inflamed intestinal follicles.

Case 37** (Taupin, Journ des Connaiss. Med. et Chir., 1839-40).—Aged seven months.

Case 38* (Schädler [quoted by Gerhardt, Handb. d. Kinderkr., 1877, ii. 373]).—Aged seven months; mother died of typhoid, nursing child previously; fever, diarrhœa, tympanites, vomiting, convulsions; duration eleven days; death. Autopsy: enlarged spleen, ulcerated Peyer's patches.

Case 39* (Hérard, L'Union Méd., 1855, ix. 365).—Aged seven months; mother died of typhoid, had nursed child, brother also with typhoid; diarrhœa, vomiting, cough, fever; death. Autopsy: enlarged spleen, intestinal follicles and mesenteric glands.

Case 40** (Hauner, Beiträge zu Pediatrik, 1863, 45).—Aged seven months; death. Autopsy: typical lesions.

Case 41** (Rilliet and Barthez, Traité Clin. des Mal. des Enf., 1861, ii. 713).—Aged seven months.

Case 42** (Ibid.).—Aged seven months.

Case 43* (E. Henoch, Charité-Annalen, 1875, ii. 540).—Aged seven months; fever, diarrhœa, cough; death. Autopsy: enlarged spleen, one swollen Peyer's patch.

Case 44 (L. Römheld, Jahrb. f. Kinderheilk., 1898, xlviii. 198).—Female, aged seven months; five other cases in house; fever, diarrhœa, tympanites; duration, seventeen days; death. Autopsy: enlarged spleen, typhoid bacilli found.

Case 45 (J. P. Crozer Griffith, Philadelphia Medical Journal, October 15, 1898). Case 2. Table I.—Male, aged seven months; fever (105°), diarrhœa, vomiting, eruption, tympanites; duration, two weeks; death.

Case 46 (P. Boobbyer, British Medical Journal, 1889, i. 187).—Aged eight months; mother with typhoid, nursing child; fever, diarrhœa; duration ten days; recovery.

Case 47 (F. R. England, Canada Medical Record, 1890, xix. 25).—Aged eight months; three other cases in house, bottle-fed infant; fever (104°), diarrhœa, eruption, cough, tympanites, enlarged spleen; duration twenty days; recovery.

Case 48 (A. Jacobi, Pediatrics, 1899, viii. 530).—Aged eight months; noma.

Case 49 (Netter, Bull. de la Soc. de Pédiat. de Paris, 1900, 2).—Aged eight months; epidemic; Widal reaction positive; duration nine days; death.

Case 50 (Ibid.).—Eight months; epidemic; Widal reaction positive; duration sixteen days; death.

Case 51 (M. C. T. Love, Journal of the American Medical Association, 1901, 893).—Female, aged eight months; two other cases in house, breast-fed child; fever (104°); eruption; Widal reaction positive; duration twenty-one days; recovery.

Case 52 (J. M. Taylor, Philadelphia Polyclinic, 1896, v. 286).—Male, aged eight and a half months; thirteen other cases in house; fever (104°), diarrhœa, tympanites, eruption; duration fifteen days; recovery.

Case 53** (E. Friedrich, Der Abdominaltyphus der Kinder., 1856, 8).—Male, aged nine months; clinically typhoid; recovery.

Case 54* (Lederer, Wien. med. Wochenschr., 1857, 196).—Male, aged nine months; epidemic; clinically typhoid.

Case 55** (Vibert, Ann. d'Hyg., 1881, vi. 353).—Male, aged nine months; previously healthy child; sudden death. Autopsy: enlarged Peyer's patches and mesenteric glands, spleen very large.

Case 56 (E. Chenery, Journal of the American Medical Association, 1891, xvi. 463).—Aged nine months; mother and eight others in house with typhoid, child nursing; typical symptoms; recovery.

Case 57 (Hölscher, Münch. med. Wochenschr., 1891, 43).—Female, aged nine months.

Case 58 (J. R. Fuller, Lancet, 1891, ii. 1038).—Female, aged nine months; another case in house; fever (102°), diarrhœa, tympanites, no eruption; duration five days; death. Autopsy: inflamed Peyer's patches, enlarged mesenteric glands and spleen.

Case 59 (H. E. Munn, Columbus Medical Journal, 1894–95, xiii. 52).—Male, aged nine months; epidemic, child bottle-fed; duration two weeks; recovery.

Case 60 (W. L. Stowell, Medical Record, 1895, xlvii. 321).—Female, aged nine months; epidemic.

Case 61 (W. P. Northrup, Medical Age, xviii., No. 9).—Female, aged nine months; other cases in house, exposed to contagion three weeks; fever (103°), diarrhœa, enlarged spleen, eruption; Widal reaction positive; duration twenty-four days; recovery.

Case 62 (A. B. Marfan, Traité des Malad. de l'Enf., i. 308).—Male, aged nine months; fever, diarrhœa, eruption, enlarged spleen; death. Autopsy: ulcerated Peyer's patches.

Case 63 (E. B. Montgomery, Medical News, 1899, lxxii. 553).—Female, aged nine months; partly bottle-fed; fever (105°), vomiting, tympanites, diarrhœa, convulsions; no leucocytosis; duration five weeks; recovery.

Case 64 (Méry, Bull. de la Soc. de Pédiat. de Paris, 1900, 22).—Aged nine months; partly breast-fed; fever; Widal reaction positive; duration two weeks; recovery.

Case 65** (Bricheteau, Gaz. Méd. de Paris, 1841, ix. 702).—Aged ten months; fever, diarrhœa; death. Autopsy: typical lesions.

Case 66** (Rilliet and Barthez, Traité Clin. des Malad. des Enf., 1861, ii. 713).—Aged ten months.

Case 67** (Lüschner, Prager Vierteljahrschr., 1846, ix. 6).—Aged ten months; mother with typhoid; death. Autopsy: typical lesions.

Case 68 (W. B. West, Texas Medical Journal, 1892-93, viii. 135).—Male, aged ten and a half months; epidemic; fever (103°), tympanites, diarrhœa, cough, eruption; duration twenty-five days; recovery.

Case 69 (H. Leroux, La France Méd., 1889, i. 517).—Female, aged eleven months; taking cow's milk three weeks; fever, vomiting, diarrhœa, tympanites, eruption; duration three weeks; recovery.

Case 70 (W. B. Noyes, Medical Record, 1894, xlvi. 1).—Male, aged eleven months; epidemic, child on milk; fever (104°), diarrhœa, eruption, cough, vomiting, collapse; duration twenty-two days; death.

Case 71 (Ibid.).—Male, aged eleven months; another case in house; fever (102°), tympanites, diarrhœa, eruption; duration sixteen days; recovery.

Case 72 (Nobécourt and Bertherand, Bull. de la Soc. de Pédiat. de Paris, 1900, 195).—Male, aged eleven months; mother with typhoid; fever, cough, tympanites, albuminuria; Widal reaction positive; death. Autopsy; typical lesions.

Case 73 (A. D. Blackader, Arch. of Pediat., 1900, xvii. 641).—Aged eleven months; several cases in family, milk infection; fever (103°), enlarged spleen, eruption, diarrhœa; duration three weeks; recovery.

Cases 74 to 80 (Vogel, Lehrb. der Kinderkr., 1890, 152).—Under twelve months.

Cases 81 and 82 (H. Lebert, Deutsch. Archiv für klin. Med., 1870, vii. 487.—Males under twelve months; epidemic.

Cases 83 and 84 (Steffen, Lehrb. der Kinderkr.).—Under twelve months; epidemic.

Case 85 (M. Röth, Arch. für Kinderheilk., 1881, ii. 365).—Under twelve months; epidemic.

Cases 86 and 87 (Von Starck, Berlin. klin. Wochenschr., 1885, xxii. 621).—Males under twelve months; epidemic.

Cases 88 to 91 (Pennsylvania Board of Health, 1885 [quoted by W. B. Noyes, Journal of American Medical Association, 1895, xxv. 530]).—Under twelve months; epidemic.

Cases 92 and 93 (J. F. Goodhart, Diseases of Children, Starr, 1889, 328).—Under twelve months; two deaths. Autopsy: diagnosis confirmed.

Cases 94 to 98 (I. Rudisch, Mt. Sinai Hospital Reports, 1899, quoted by A. Jacobi [Pediat., 1899, viii. 546]).—Under twelve months; three died, two recovered.

Cases 99 to 134* (Brouardel, Rec. du Comité Consult. d'Hyg., 1891).—Under twelve months; deaths in all. Autopsy: typical lesions.

Case 135 (W. B. Noyes, Journal of the American Medical Association, 1895, xxv. 529).—Male, under twelve months; epidemic.

Cases 136 to 138 (Berg, Deutsch. Arch. f. klin. Med. 1895, liv. 161).—Under twelve months; epidemic.

Case 139 (L. Römheld, Jahrb. f. Kinderheilk., 1898, xlviii. 198).—Under twelve months; epidemic.

Of the 139 reported cases, not congenital, occurring in the first year and collected in the preceding table, 111 may reasonably be considered typhoid fever; 46 (marked*) are doubtful, yet are probably instances of the disease; 17 (marked**) are doubtful, and seem to us probably not cases of typhoid fever; 24 are males, 15 females, and in 100 the sex is not mentioned; 52 occurred in general or house epidemics, in 14 of these the mothers having typhoid, and in 14 cases there being other cases not mentioned as the mother, or in addition to her. Fever was noted in 46, diarrhœa in 42, constipation in 1, eruption in 26, enlarged spleen in 26, tympanites in 18, vomiting in 11, collapse in 3, cough in 5, pneumonia in 1, noma in 1, convulsions in 4, hemorrhage in 1, otitis in 1, relapse in 1, and albuminuria in 1.

Recovery is noted in 28, death in 77, and the result is not mentioned in 34.

Of the 77 fatal cases, typhoid bacilli were reported in 2 cases only.

A positive Widal reaction was reported in 8 cases.

In the next table (Table V.) are included cases of typhoid fever in the second year of life—*i. e.*, in children of one year up to but not including the age of two years.

Table V. Typhoid Fever in the Second Year of Life.

Case 1* (A. Flint, American Journal of Medical Sciences, 1845, x. 28).—Female, aged twelve months; epidemic, two other cases in house; fever, constipation, cough; recovery.

Case 2 (W. Diem, Jahrb. f. Kinderheilk., 1882, xviii. 270).—Female, aged twelve months; epidemic, taking cow's milk; fever, diarrhœa, eruption, cough, enlarged spleen, otitis media, convulsions; duration four weeks; recovery.

Case 3 (Parrot, Prog. Méd., 1883, xi. 467).—Aged twelve months; typical illness, with relapse; recovery.

Case 4 (J. W. Long, Arch. of Pediat., 1893, x. 53).—Male, aged twelve months; mother died of typhoid, father and eight others in house with it; fever (104.5°), cough, tympanites, constipation followed by diarrhœa; recovery.

Case 5 (Griffith and Ostheimer).—Case 3, Table I.—Male, aged twelve months; diarrhœa, fever (100.8°), tympanites, cough, eruption.

Case 6 (W. L. Stowell, Medical Record, 1895, xlvii. 321).—Female, aged twelve months; both parents with typhoid; cough, fever, diarrhœa; duration ten days; recovery.

Case 7 (Ibid.).—Male, aged twelve months; epidemic, taking milk; fever (105°), eruption, convulsions; duration twenty-two days; death.

Case 8** (C. M. Billard, Traité des Malad. des Enf., 1835, 229).—Male, aged thirteen months; fever, diarrhœa, tympanites, vomiting, collapse; death. Autopsy: ulcerated Peyer's patches.

Case 9** (Rilliet, Thèse de Paris, 1840).—Aged thirteen months.

Case 10 (W. L. Stowell, Medical Record, 1895, xlvii. 321).—Female, aged thirteen months; epidemic; fever (105.5°), eruption, diarrhœa, enlarged spleen, meningeal symptoms; duration nineteen days; recovery.

Case 11 (W. P. Northrup, Arch. of Pediat., 1896, xiii. 11).—Aged thirteen months; father and brother in house with typhoid; breast- and bottle-fed; milk epidemic; fever (104°), constipation, enlarged spleen, eruption; duration thirteen days; recovery.

Case 12 (Howell, Transactions of the Luzerne County Medical Society, 1896, 91).—Aged thirteen months; epidemic.

Case 13 (E. C. Seufert, New York Medical Journal, 1899, lxx. 233).—Aged thirteen months; enlarged spleen, fever, eruption; Widal reaction positive; duration fourteen days; recovery.

Case 14 (A. D. Blackader, Archiv. of Pediat., 1900, xvii. 641).—Aged thirteen months; fever, cough, diarrhœa, enlarged liver and spleen, tympanites; Widal reaction negative; duration five days; death. Autopsy: typical lesions, typhoid bacilli found.

Case 15 (W. P. Northrup, Archiv. of Pediat., 1900, xvii. 651).—Aged thirteen months; eruption.

Case 16 (J. L. Morse, Arch. of Pediat., 1900, xvii. 894).—Aged thirteen months; mother with typhoid, child taking milk; diarrhœa, eruption, enlarged spleen; Widal reaction positive; duration three weeks; recovery.

Case 17 (W. S. Lazarus-Barlow, British Medical Journal, 1901, ii. 792).—Male, aged thirteen months; five other cases in house; eruption, diarrhœa, tympanites, cough; Widal reaction positive; duration twenty-five days; death. Autopsy: enlarged spleen, typhoid bacilli, no intestinal lesions.

Case 18 (Chambard-Henon, Lyon Méd., 1897, lxxxiv. 409).—Female, aged thirteen and a half months; child taking breast milk and water; fever (104°), vomiting, diarrhœa, cough, eruption; duration twenty days; recovery.

Case 19* (Bernheim, Leçons Cliniques, 1877).—Aged fourteen months; diarrhœa; death. Autopsy: enlarged spleen, Peyer's patches, and mesenteric glands.

Case 20 (M. Röth, Arch. f. Kinderheilk., 1881, ii. 365).—Female, aged fourteen months; epidemic; fever (104°), epistaxis, convulsions; relapse; duration six weeks; recovery.

Case 21 (Mercier, Allg. Wien. med. Zeit., 1895, xl. 516).—Aged fourteen months; milk infection; fever, diarrhœa, eruption, enlarged spleen, tympanites; duration thirteen days; recovery.

Case 22 (G. J. Martz, Cleveland Medical Gazette, 1896-97, xii. 510).—Male, aged fourteen months; three months after weaning; epistaxis, enlarged spleen, fever (103.5°), desquamation; duration twenty-seven days; recovery.

Case 23 (H. A. Fairbairn, Journal of the American Medical Association, 1897, xxix. 1149).—Aged fourteen months.

Case 24 (W. P. Northrup, Archiv. of Pediat., 1900, xvii 651).—Aged fourteen months; other cases in house, child nursing

Case 25 (Nobécourt and Bertherand, Bull. de la Soc. de Pédiat. de Paris, 1900, 195).—Female, aged fourteen months; five other cases in house; fever, diarrhœa, tympanites, eruption; Widal reaction positive; duration two weeks; recovery.

Case 26 (Griffith and Ostheimer).—Case 4, Table I.—Female, aged fourteen months; fever (106°), tympanites, diarrhœa, eruption; relapse; duration five weeks; death.

Case 27** (Bierbaum [quoted by Gerhardt, Handb. d. Kinderkr., 1877, ii. 374]).—Aged fifteen months; typical symptoms; relapse.

Case 28 (A. D. Walker, British Medical Journal, 1879, i. 347).—Aged fifteen months; mother developed typhoid one week after child; fever, diarrhœa, eruption, tympanites; recovery.

Case 29 (X. E. Wagner, Deutsch. Arch. f. klin. Med. 1882–83, xxxii. 288).—Male, aged fifteen months; four other cases in house; fever, diarrhœa; duration two weeks; death Autopsy: typical lesions found.

Case 30 (B. Lewy, Arch. f. Kinderheilk., 1888–89, x. 81).—Male, aged fifteen months; fever, diarrhœa, laryngeal ulceration, convulsions; duration eight days; death. Autopsy: enlarged spleen and mesenteric glands, ulcerated Peyer's patches, typhoid bacilli and staphylococci found.

Case 31 (A. B. Marfan, Traité des Mal. de l'Enf., i. 318).—Aged fifteen months; death.

Case 32 (Cadet de Gassicourt, Rév. Mens. des Mal. de l'Enf., 1890, 204).—Aged fifteen months.

Case 33 (W. O. Bridges, New York Medical Record, 1896, xlix. 428).—Aged fifteen months; typhoid in milkman's family; fever (104.6°), epistaxis, diarrhœa, cough, enlarged spleen; duration twenty days; recovery.

Case 34 (C. Kasel and K. Mann, Münch. med. Wochenschr., 1899, xlvi. 581).—Male, aged fifteen months; two other cases in house; typical "symptoms;" Widal reaction positive; recovery.

Case 35 (Griffith and Ostheimer).—Case 5, Table I.—Male, aged fifteen months; three other cases in house; fever (105°), diarrhœa, cough, eruption; Widal reaction positive; duration three weeks; recovery.

Case 36 (Cadet de Gassicourt, Rév. Mens. des Mal. de l'Enf., 1890, 204).—Aged sixteen months.

Case 37 (Goldberger, Aerztes Cent.-Anzeig., 1896, viii. 209).—Aged sixteen months.

Case 38 (J. I. Roe, Transactions of the Luzerne County Medical Society, 1896, 91).—Aged sixteen months; both parents with typhoid; recovery.

Case 39 (W. P. Northrup, Arch. of Pediat., 1896, xiii. 11).—Female, aged sixteen months; another case in house, milk epidemic; fever (104°), diarrhœa, eruption; recovery.

Case 40 (E. C. Seufert, New York Medical Journal, 1899, lxx. 233).—Aged sixteen months; enlarged spleen, eruption; Widal reaction positive; duration sixteen days; recovery.

Case 41 (F. Sbrana, Arch. de Méd. des Enf., 1899, ii. 29).—Aged sixteen months; epidemic.

Case 42 (Netter, Bull. de la Soc. de Pédiat. de Paris, 1900, 2).—Aged sixteen months; Widal reaction positive; duration fifteen days; recovery.

Case 43 (A. D. Blackader, Arch. of Pediat., 1900, xvii. 641).—Aged sixteen months; other cases in house, milk infection; fever (104°), diarrhœa, enlarged spleen; duration three weeks; recovery.

Case 44 (A. A. Strasser, Medical Record, 1901, lx. 286).—Female, aged sixteen months; fever, constipation, enlarged spleen; relapse; duration five weeks; recovery.

Case 45 (E. F. Brush, New York Medical Journal, 1902, lxxv. 583).—Aged sixteen months; mother with typhoid, child given water; recovery.

Case 46 (W. L. Stowell, New York Medical Record, 1895, xlvii. 321).—Female, aged seventeen months; mother with typhoid, milk epidemic; fever (105°), relapse; duration five weeks; recovery.

Case 47 (Netter, Bull. de la Soc. de Pédiat. de Paris, 1900, 2).—Aged seventeen months; recovery.

Case 48** (Bürkner [quoted by Gerhardt, Handb. d. Kinderkr., 1877, ii. 373)].—Aged eighteen months; high fever.

Case 49 (H. N. Reed, Brooklyn Medical Journal, 1888–89, iii. 599).—Female, aged eighteen months; fever (105.5°), diarrhœa, eruption, tympanites; duration four weeks; recovery.

Case 50 (J. E. Reeves, Transactions of the Association of American Physicians, 1890, v. 18).—Aged eighteen months; mother with typhoid.

Case 51 (Cadet de Gassicourt, Rév. Mens. des Mal. de l'Enf., 1890).—Aged eighteen months.

Case 52 (J. R. Fuller, Lancet, 1891, ii. 1038).—Aged eighteen months; another case in house; fever, diarrhœa, vomiting; recovery.

Case 53 (Huber, Arch. of Pediat., 1892, ix. 763).—Aged eighteen months; five other cases in house.

Case 54 (Ibid.).—Aged eighteen months; five other cases in house.

Case 55 (W. B. Noyes, Medical Record, 1894, xlvi. 1).—Female, aged eighteen months; two other cases in house, epidemic; fever, constipation, cough, no eruption; duration twenty-eight days; recovery.

Case 56 (I. N Love, Journal of the American Medical Association, 1895, xxiv. 1).—Female, aged eighteen months; fever (105°), diarrhœa, vomiting; duration ten days; death. Autopsy: marked ulceration of Peyer's patches.

Case 57 (W. O. Bridges, New York Medical Record, 1896, xlix. 428).—Aged eighteen months; fever, eruption, enlarged spleen; duration three weeks; recovery.

Case 58 (Howell, Transactions of the Luzerne County Medical Society, 1896, 91).—Aged eighteen months; epidemic.

Case 59 (G. Hadot, Rév. Méd. de l'Est., 1896, xxviii. 468).—Aged eighteen months; epidemic; Widal reaction positive.

Case 60 (Haushalter, Rév. Méd. de l'Est., 1896, xxviii. 750).—Aged eighteen months; epidemic; typical symptoms; Widal reaction positive.

Case 61 (A. B. Marfan, Traité des Mal. de l'Enf., i. 333).—Male, aged eighteen months; weaned at three months; fever, diarrhœa, vomiting, tympanites, eruption, convulsions; recovery.

Case 62 (J. C. Wilson, Keating's Cyclopædia of Diseases of Children, 1899, v. 168).—Aged eighteen months.

Case 63 (From Long Island College Hospital, Yale Medical Journal, 1899, vi. 95).—Aged eighteen months; mother and sister with typhoid; eruption, enlarged spleen; Widal reaction positive; duration twenty days; recovery.

Case 64 (A. Samuels, New York Medical Journal, 1900, lxxii. 4).—Aged eighteen months; aphasia during last week of fever, constipation, enlarged spleen, typhoid bacilli in feces; Widal reaction positive; duration twenty days; recovery.

Case 65 (A. D. Blackader, Arch. of Pediat., 1900, xvii. 641).—Aged eighteen months; epidemic; eruption, diarrhœa, tympanites, enlarged spleen; duration sixteen days; recovery.

Case 66 (Netter, Bull. de la Soc. de Pédiat. de Paris, 1900, 2).—Aged eighteen months; fever; duration twenty-eight days; recovery.

Case 67 (Haushalter, Gaz. Hebd. de Méd. et de Chir., 1901, N. S. 6, xlviii. 321).—Female, aged eighteen months; vomiting, diarrhœa, tympanites, eruption, laryngeal ulceration, with tracheotomy; death. Autopsy: characteristic lesions.

Case 68 (M. Gershel, New York Medical Record, 1901, lx. 811).—Aged eighteen months; Widal reaction positive.

Case 69** (Med.-Chirurg. Rev., 1858, [quoted by Stowell Medical Record, 1898, xlvii. 324]).—Aged nineteen months.

Case 70 (J. P. Crozer Griffith, Philadelphia Medical Journal, October 15, 1898).—Case 6, Table I.—Female, aged nineteen months; fever (104°), diarrhœa, cough, enlarged spleen, eruption; Widal reaction positive; duration four weeks; recovery.

Case 71 (J. P. Crozer Griffith, Philadelphia Medical Journal, October 15, 1898).—Case 7, Table I.—Male, aged nineteen months; diarrhœa, cough, fever (102°), enlarged spleen, eruption, diphtheria; Widal reaction positive; recovery.

Case 72 (A. A. Strasser, Medical Record, 1901, lx. 286).—Female, aged nineteen months; fever, cough, constipation; Widal reaction positive; recovery.

Case 73 (Kissel, Dietsk. Med., Moscow, 1896, i. 118).—Aged twenty months; perforation.

Case 74 (G. J. Martz, Cleveland Medical Gazette, 1896-97, xii. 510).—Male, aged twenty months; another case in house; fever, tympanites, no eruption or epistaxis; duration twenty-seven days; recovery.

Case 75 (Barbier and Herrenschmidt, Gaz. des Malad. Inf., 1899, i. 408).—Male, aged twenty months; duration twenty-four days; recovery.

Case 76* (E. Henoch, Charité-Annalen, 1875, ii. 540).—Female, aged twenty-one months; developed diphtheria during convalescence; death.

Cases 77 and 78 (Archambault, Gaz. Méd. de Paris, 1880, 6 s. ii. 42).—Aged twenty-one months.

Case 79 (F. D. Drewitt, British Medical Journal, 1894, ii. 809).—Male, aged twenty-one months; another case in house a month before; vomiting, cough, tympanites, perforation, no eruption or enlarged spleen; duration three weeks; death. Autopsy: ulcerated perforated Peyer's patch found.

Case 80 (J. M. O'Malley, University Medical Magazine, 1896-97, 636).—Case 8, Table I.—Female, aged twenty-one months; two other cases in house; fever (106°), diarrhœa, tympanites, eruption; duration twenty-three days; recovery.

Case 81 (J. H. Bryant, British Medical Journal, 1899, i. 776).—Male, aged twenty-one months; two other cases in house; fever (105°), diarrhœa, vomiting, tympanites, cough, enlarged spleen; Widal reaction positive; duration twenty-two days; death. Autopsy: typhoid bacilli cultivated from intestinal lesions.

Case 82** (Littré. Dictionnaire. Article on "Dothiénentérie," 1835).—Aged twenty-two months; recovery.

Case 83** (Rilliet and Barthez, Arch. Gén. de Méd., 1840, 3 s. ix. 155).—Male, aged twenty-two months; fever, diarrhœa; duration seventeen days; death. Autopsy: typical lesions.

Case 84** (Bricheteau, Gaz. Méd. de Paris, 1841, ix. 702).—Aged twenty-two months; recovery.

Case 85 (Rilliet and Barthez, Traité Clin. des Mal des Enf., 1891, iii. 352).—Aged twenty-two months; laryngeal ulceration with tracheotomy; duration five days; death. Autopsy: enlarged mesenteric glands and solitary follicles, with ulcers.

Case 86 (W. P. Northrup, Arch. of Pediat., 1896, xiii. 11).—Male, aged twenty-two months; mother with typhoid, milk epidemic; fever (104.5°), eruption, cough, enlarged spleen, diarrhœa; death. Autopsy: swollen Peyer's patches, follicles, mesenteric glands and spleen.

Case 87 (Ibid.).—Aged twenty-two months; other cases of typhoid in house, milk epidemic; fever (105°), eruption, diarrhœa, enlarged spleen, cough, tympanites; duration fifteen days; recovery.

Case 88 (G. J. Martz, Cleveland Medical Gazette, 1896-97, xii. 510).—Female, aged twenty-two months; another case in house; fever, diarrhœa, eruption, epistaxis, intestinal hemorrhage, parotitis; duration seventeen days; recovery.

Case 89 (F. Nachod, Prager med. Wochenschr., 1897, xxii. 528).—Male, aged twenty-two months; two other cases in house; fever, cough, diarrhœa, enlarged spleen; Widal reaction positive; duration four weeks; death. Autopsy: enlarged spleen and mesenteric glands, no intestinal lesions.

Case 90 (W. L. Stowell, Medical Record, 1895, xlvii. 321).—Aged twenty-two months; other cases in house, epidemic; duration six weeks; recovery.

Case 91 (Netter, Bull. de la Soc. de Pédiat. de Paris, 1900, 2).—Aged twenty-two months; Widal reaction positive; duration eleven days; recovery.

Case 92 (H. A. Fairbairn, Journal of the American Medical Association, 1897, xxix. 1149).—Aged twenty-three months.

Case 93 (J. P. Crozer Griffith, Philadelphia Medical Journal, October 15, 1898).—Case 9, Table I.—Male, aged twenty-three months; mother with typhoid; fever (104.8°), vomiting, diarrhœa, cough, tympanites; no eruption or enlarged spleen; duration six weeks; recovery.

Case 94** (Friedleben, Arch. physiolog. Heilk., 1848, xlix. 28).—Male, under two years; death.

Cases 95 to 97* (E. Friedrich, Der Abdominaltyphus der Kinder., 1856, 8).—Males, under two years; epidemic; one death, two recoveries.

Cases 98 to 102* (Ibid.).—Females, under two years; epidemic; two deaths, three recoveries.

Cases 103 to 109* (Lederer, Wien. med. Wochenschr., 1857, 196).—Under two years; epidemic.

Case 110* (E. Henoch, Charité-Annalen, 1875, ii. 540).—Under two years.

Cases 111 and 112 (M. Röth, Arch. f. Kinderheilk., ii. 365).—Under two years; epidemic.

Cases 113 to 126 (Pennsylvania State Board of Health Report, 1885, quoted by W. B. Noyes, Journal of American Medical Association, 1895, xxv. 530).—Under two years; epidemic.

Cases 127 to 141 (G. de Montmollin, Thèse de Neuchatel, 1885).—Under two years; epidemic.

Cases 142 and 143 (Von Starck, Berlin. klin. Wochenschr., 1885, xxii. 621).—Males, under two years; epidemic.

Cases 144 and 145 (Ibid.).—Females, under two years; epidemic.

Case 146 (H. Schultz, Jahrb. der Hamburger Staatskr. Anstalt., 1889).—Male, under two years; epidemic.

Cases 147 to 152 (Ibid.).—Females, under two years; epidemic.

Case 153 (J. F. Goodhart, Diseases of Children, Starr, 1889, 328).—Under two years.

Case 154 (Bergquist, Eira, 1895, xix. 11).—Under two years.

Cases 155 and 156 (Berg, Deutsch. Arch. f. klin. Med., 1895, liv. 161).—Under two years; epidemic.

Cases 157 to 159 (Ollivier, Leçons Clin. sur les Malad. des Enf., 355).—Under two years; two deaths, one recovery.

Cases 160 to 164 (L. Römheld, Jahrb. f. Kinderheilk., 1898, xlviii. 198).—Under two years.

Cases 165 to 170 (I. Rudisch, Mt. Sinai Hospital Report, 1899, quoted by A. Jacobi, Pediatrics, 1899, viii. 546).—Under two years; six recoveries.

Case 171 (F. Sbrana, Arch. de Méd. des Enf., 1899, ii. 29).—Under two years; epidemic.

Cases 172 to 187 (T. M. Rotch, Arch. of Pediat., 1900, xvii. 653).—Under two years; eight deaths, eight recoveries.

Of the 187 cases occurring in the second year of life collected in the preceding table, 171 may reasonably be considered typhoid fever; 7 (marked*) are doubtful, yet are probably instances of the disease; 7

(marked**) are doubtful, and seem to us probably not cases of typhoid fever; 26 are males, 34 females, and in 127 the sex is not mentioned; 101 occurred in general or house epidemics, in 11 of these the mothers having typhoid, and in 32 cases there being other cases in the house, not mentioned as the mother, or in addition to her. Fever was observed in 50, diarrhœa in 40, constipation in 6, eruption in 27, enlarged spleen in 26, tympanites in 18, vomiting in 9, collapse in 1, cough in 20, convulsions in 6, hemorrhage in 1, relapse in 6, parotitis in 1, meningeal symptoms in 1, perforation in 2, desquamation in 1, epistaxis in 4, aphasia in 1, laryngeal ulceration in 2, otitis in 1, and diphtheria in 2.

Recovery was noted in 69, death in 32, while the result in 86 was not mentioned.

Of the 32 fatal cases, typhoid bacilli were found in 3 cases only. In 1 case they were present in the feces in a child who recovered.

A positive Widal reaction was recorded in 19 cases. In 1 case the reaction was negative during life, though typhoid bacilli were cultivated post-mortem.

In the final table (Table VI.) we have placed the cases of typhoid fever in the third year of life up to and including the age of two and a half years. After that age the number reported multiplied so rapidly that we decided not to extend our investigations beyond it.

TABLE VI. TYPHOID FEVER IN THE THIRD YEAR OF LIFE UP TO THE AGE OF TWO AND A HALF YEARS.

Case 1** (Rilliet and Barthez, Arch. Gén. de Méd., 1840, 3 s. ix. 155).—Male, aged two years; fever, diarrhœa, vomiting; duration forty-three days; death. Autopsy: typical lesions.

Case 2** (Ibid.).—Male, aged two years; fever, diarrhœa, vomiting; duration over two months; death. Autopsy: typical lesions.

Case 3** (Taupin, Journ. des Connaiss. Med. et Chir., 1840, 198).—Aged two years.

Cases 4 to 11* (Lederer, Wien. med. Wochenschr., 1857, 196).—Aged two years; epidemic.

Case 12** (Med.-Chirurg. Rev., 1858 [quoted by Stowell]).—Medical Record, 1895, xlvii. 324 Male, aged two years.

Case 13* (Fiedler, Arch. f. Kinderheilk., 1862, iii. 155).—Female, aged two years; epidemic; recovery.

Case 14 (A. Jacobi, Arch. of Pediat., 1885, ii. 129).—Aged two years.

Case 15 (A. E. Okey, Peoria Medical Monthly, 1886–87, vii. 419).—Female, aged two years; nine other cases in house; recovery.

Case 16 (L. H. Taylor, Annals of Hygiene, 1892, vii. 393).—Male, aged two years; other cases in house, milk infection; typical symptoms; death.

Case 17 (Ibid.).—Male, aged two years; epidemic, milk infection; recovery.

Case 18 (A. Moussous, Arch. Clin. de Bordeaux, 1892, i. 149).—Aged two years; epidemic; fever, phlegmasia alba dolens, convulsions; duration thirty-four days; death.

Case 19 (C. Vouillemin, Thèse de Nancy, 1892, 12).—Female, aged two years; fever, diarrhœa, vomiting, tympanites, eruption; recovery.

Case 20 (Ibid.).—Aged two years.

Case 21 (S. S. Adams, American Journal of Obstetrics, 1895, xxxi. 175).—Female, aged two years; fever (105°), diarrhœa, cough, relapse; death. Autopsy: typical lesions, typhoid bacilli found.

Case 22 (Haushalter, Rév. Méd. de l'Est., 1895, xxvii. 246).—Aged two years; epidemic; fever; duration eleven days; recovery.

Case 23 (D. R. Emmons, Cincinnati Lancet-Clinic, 1895, n. s. xxxiv. 91).—Female, aged two years; fever (105°), tympanites, convulsions; duration two weeks; recovery.

Case 24 (W. B. Stowell, Medical Record, 1895, xlvii. 321).—Male, aged two years; epidemic: fever (103°), eruption; duration three weeks; recovery.

Case 25 (W. P. Northrup, Arch. of Pediat., 1895, xii. 57).—Aged two years; mother with typhoid; fever (105°), enlarged spleen, eruption; duration five weeks; recovery.

Case 26 (Griffith and Ostheimer).—Case 10, Table I.—Female, aged two years; fever (103.6°), vomiting, tympanites, cough, diarrhœa, enlarged spleen, eruption; duration thirty-two days; recovery.

Case 27 (S. S. Adams, American Journal of Obstetrics, 1896, xxxiii. 720).—Female, aged two years; fever (105°), vomiting, tympanites, diarrhœa, cough, meningeal symptoms; duration four weeks; recovery.

Case 28 (E. Henoch, Vorlesung. ü. Kinderkr., 1897, 771).—Female, aged two years; "typical symptoms;" duration fourteen days; death. Autopsy: enlarged Peyer's patches.

Case 29 (L. Römheld, Jahrb. f. Kinderheilk., 1898, xlviii. 198).—Male, aged two years; father with typhoid; fever, cough, tympanites; duration twenty-four days; death. Autopsy: typhoid bacilli found.

Case 30 (Griffith and Ostheimer).—Case 11, Table I.—Male, aged two years; fever (104°), cough, vomiting, enlarged spleen, eruption; recovery.

Case 31 (J. C. Thresh and E. R. Walter, British Medical Journal, 1899, ii. 1669).—Male, aged two years; recovery.

Case 32 (G. Cagliari, Journal of the American Medical Association, 1899, xxxii. 881) —Aged two years; others in house with typhoid; "clinically typical."

Case 33 (A Jacobi, Pediatrics, 1899, viii. 530).—Aged two years; hemorrhage.

Case 34 (C. Kasel and K. Mann, Münch. med. Wochenschr., 1899, xlvi. 581).—Aged two years; Widal reaction positive; recovery.

Case 35 (J. Comby, Bull. de la Soc de Pédiat. de Paris, 1900, 65).—Aged two years; death.

Case 36 (Netter, Bull. de la Soc. de Pédiat. de Paris, 1900, 2).—Aged two years; duration twenty-one days; recovery.

Case 37 (J. F. Bell, Arch. of Pediat., 1901, xviii. 345).—Aged two years; another case in house; fever, diarrhœa; Widal reaction positive; duration two weeks; recovery.

Case 38 (Ibid.) —Male, aged two years; case of typhoid next door; fever (103°), diarrhœa, vomiting, enlarged spleen, eruption; Widal reaction positive; duration twenty-eight days; recovery.

Case 39 (Griffith and Ostheimer).—Case 12, Table I.—Male, aged two years; brother in house with typhoid; fever (103.4°), diarrhœa, tympanites, eruption; Widal reaction positive; duration twenty-two days; recovery.

Case 40 (A. O. J. Kelly, Pediatrics, 1897, iv. 37).—Aged two years one month; mother with typhoid; fever, diarrhœa, enlarged spleen, tympanites, eruption; recovery.

Case 41 (W. P. Northrup, Arch. of Pediat., 1896, xiii. 11).—Female, aged two years three months; five other cases in house, milk infection; cough, eruption, alternate constipation and diarrhœa; recovery.

Case 42 (Griffith and Ostheimer).—Case 13, Table I.—Female, aged two years three months; fever (102.5°), diarrhœa, enlarged spleen, tympanites, eruption, scarlatina; Widal reaction positive.

Case 43 (J. P. Crozer Griffith, Philadelphia Medical Journal, October 15, 1898).—Case 14, Table I.—Female, aged two years four months; mother and brother with typhoid; fever (105°), diarrhœa, enlarged spleen, pneumonia; duration ten days; death. Autopsy: enlarged spleen mesenteric glands and Peyer's patches, slight ulceration.

Case 44 (W. L. Stowell, Medical Record, 1895, xlvii. 321).—Aged two years five months; other cases in house, epidemic; eruption; recovery.

Case 45 (Griffith and Ostheimer.)—Case 15, Table I.—Male, aged two years five months; fever (105°); Widal reaction positive; duration two weeks; recovery.

Case 46 (A. Kühn, Deutsch. Arch. f. klin. Med., 1876, xvii. 221).—Male, aged two and a half years; fever, diarrhœa, cough, eruption, enlarged spleen; recovery.

Case 47 (M. Röth, Arch. f. Kinderheilk., 1881, ii. 365).—Male, aged two and a half years; fever, meningeal symptoms, pneumonia; duration five days; death. Autopsy: typical lesions.

Case 48 (P. Kohlstock, Berlin Thesis, 1882, 10).—Female, aged two and a half years; epidemic; fever, vomiting, diarrhœa, collapse; duration three weeks; death. Autopsy: typical lesions.

Case 49 (H. N. Read, Brooklyn Medical Journal, 1888–89, iii. 599).—Male, aged two and a half years; fever (104°), diarrhœa, tympanites, eruption; duration thirty days recovery.

Case 50 (W. B. Noyes, Medical Record, 1894, xlvi. 1).—Female, aged two and a half years; milk epidemic; eruption, tympanites, fever (103°); duration two weeks; recovery.

Case 51 (Ibid.).—Female, aged two and a half years; two other cases in house, milk epidemic; fever (104°), eruption; duration two weeks; recovery.

Case 52 (J. L. Morse, Boston Medical and Surgical Journal, 1896, cxxxiv. 205).—Aged two and a half years; fever (103°), diarrhœa, eruption; duration ten days; recovery.

Case 53 (B. Boyer, Lyon Méd., 1896, lxxxiii. 361).—Male, aged two and a half years; epidemic; fever, eruption, diarrhœa, tympanites; duration four weeks; recovery.

Case 54 (W. P. Northrup, Arch. of Pediat., 1896, xiii. 11).—Female, aged two and a half years; six other cases in house; typical, mild; recovery.

Case 55 (L. Guinon, Rév. Mens. des Malad. de l'Enf., 1897, xv. 236).—Female, aged two and a half years; fever (104°), constipation, tympanites, enlarged spleen, eruption, meningeal symptoms, collapse; Widal reaction positive; duration three weeks; recovery.

Case 56 (E. Henoch, Vorlesung. ü. Kinderkr., 1897, 771).—Female, aged two and a half years; fever: relapse; duration eight weeks; death. Autopsy: typical lesions.

Case 57 (E. Rosenthal, Pediatrics, 1897, iv. 38).—Aged two and a half years; Widal reaction positive; recovery.

Case 58 (H. A. Fairbairn, Journal of the American Medical Association, 1897, xxix. 1149).—Aged two and a half years.

Case 59 (Meinecke, Münch. med. Wochenschr., 1898, xlv. 435).—Female, aged two and a half years; fever (104°); Widal reaction positive; duration seven days; death. Autopsy: typhoid bacilli found in spleen.

Case 60 (G. Cagliari, Journal of the American Medical Association, 1899, xxxii. 881).—Aged two and a half years; other cases in house; "clinically typical."

Case 61 (C. Kasel and K. Mann, Münch. med. Wochenschr., 1899, xlvi. 581).—Male, aged two and a half years; Widal reaction positive; recovery.

Case 62 (Ibid.).—Male, aged two and a half years; Widal reaction positive; recovery.

Case 63 (Barbier and Herrenschmidt, Gaz. des Malad. Inf., 1899, i. 403).—Female, aged two and a half years; fever, diarrhœa; duration twenty-two days; recovery.

Case 64 (Ibid.).—Female, aged two and a half years; fever, diarrhœa; duration seventeen days; recovery.

Case 65 (Griffith and Ostheimer).—Case 16, Table I.—Female, aged two and a half years; fever (105°), eruption, enlarged spleen, diphtheria; Widal reaction positive.

Case 66 (Griffith and Ostheimer).—Case 17, Table I.—Female, aged two and a half years; fever (106°), vomiting, tympanites, constipation, otitis, pneumonia, diphtheria; Widal reaction positive; duration four weeks; death.

Case 67 (Griffith and Ostheimer).—Case 18, Table I.—Female, aged two and a half years; brother also with typhoid; fever (103°), epistaxis, diarrhœa, tympanites, enlarged spleen, eruption; recrudescence; Widal reaction positive; duration three weeks; recovery.

Case 68 (Netter, Bull. de la Soc. de Pédiat. de Paris, 1900, 2).—Aged two and a half years; fever; duration twenty-one days; recovery.

Of the 68 cases collected in the preceding table, 55 may be fairly considered to be typhoid fever; 9 (marked*) are doubtful, yet are probably instances of the disease; 4 (marked**) are doubtful and seem to us probably not cases of typhoid fever; 19 are males, 24 females, and in 35 the sex is not mentioned; 30 occurred in general or house epidemics, in 3 of these the mothers having typhoid, and in 17 instances there being other cases in the house, not mentioned as the mother, or in addition to her. Fever was observed in 42, diarrhœa in 24, constipation in 3, eruption in 23, enlarged spleen in 13, tympanites in 12, vomiting in 8, collapse in 2, cough in 6, pneumonia in 3, convulsions in 2, hemorrhage in 1, relapse in 2, recrudescence in 1, otitis in 1, meningeal symptoms in 3, epistaxis in 1, phlegmasia alba dolens in 1, diphtheria in 2, and scarlatina in 1.

Recovery was noted in 36, death in 14, while the result in 18 cases was not mentioned.

Of the 14 fatal cases, typhoid bacilli were found in 3 cases only.

A positive Widal reaction was recorded in 14 cases.

The following summary of the cases of typhoid fever in children up to two and a half years expresses in brief the most prominent features as far as the reports, often incomplete, make these manifest:

Cases in the first year of life—congenital	23
other cases	139
Total	162
Cases in the second year of life	187
Cases from two to two and a half years inclusive	68
Total	417
Of these we must consider extremely doubtful	30
Leaving	387
Even if we subtract the doubtful yet probable cases	62
We have remaining a total of	325

Out of 153 in which the sex was known, 77 were males, 76 females. 185 are said to have occurred during general or house epidemics, in 97 of these there being other cases in the house, of which 45 occurred in the mothers.

Fever was noted in	143	Jaundice in	3
Diarrhœa in	113	Hemorrhage from the bowel in	5
Constipation in	11	Diphtheria in	4
Eruption in	78	Otitis in	3
Enlarged spleen in	71	Scarlet fever in	1
Tympanites in	50	Perforation in	2
Cough in	33	Laryngeal ulceration in	2
Pneumonia in	4	Parotitis in	1
Vomiting in	29	Recrudescence in	1
Convulsions in	14	Desquamation in	1
Meningeal symptoms in	4	Aphasia in	1
Relapse in	9	Noma in	1
Collapse in	6	Phlegmasia alba dolens in	1
Epistaxis in	5	Albuminuria in	1

A positive Widal reaction was noted in 44 cases only; in 2 cases it was negative during life, but typhoid bacilli were found post-mortem.

Of the 145 in which fever was observed, the highest temperature is recorded in 65, as follows:

	Cases.		Cases.
100° to 101°	1	103° to 104°	24
101° to 102°	3	104° to 105°	20
102° to 103°	11	105° to 106°	6

The duration is stated in 117 cases as follows:

Under one week	12	4 to 5 weeks	14
1 to 2 weeks	28	5 to 6 weeks	5
2 to 3 weeks	29	6 to 7 weeks	1
3 to 4 weeks	26	7 to 8 weeks	2

Out of 278 cases in which the result is recorded, 136 recovered, 142 died.

Out of 98 autopsies performed, typhoid bacilli were found in 14 cases.

No relative figures can be given regarding the frequency of symptoms, owing to the meagre details which attend the reports of many of

the cases. For instance, although more cases in our table are reported to have died than to have recovered, it is certain that this by no means indicates the actual relative mortality of the disease in childhood. This is partly explained by the fact that in 39 cases the result is not stated. It may be assumed that recovery took place in nearly all of these. There is also probably a greater disposition to report the fatal cases as being more unusual. The failure to recognize the milder cases has already been alluded to.

It seems to us that the main point at issue, the fact that typhoid fever is *not* so uncommon in early life as often claimed, may be considered established, not only by our own individual experience, but still more strongly by the reports of cases in medical literature.

ADDENDUM.—Since the reading of the above paper, details of at least half a dozen cases of typhoid fever in children of two years and less have been given to us by several colleagues who have not considered publication of the matter worth while. There has also occurred in the experience of one of us a well-marked and fatal case in a child of nine months. All these cases sustain the point which we have advanced, namely, that the disease is much more frequent in early life than the common belief or even published reports would indicate.

CLINICAL OBSERVATIONS ON CONGENITAL AND ACQUIRED TRANSPOSITION OF THE VISCERA.

BY JAMES RAE ARNEILL, A.B., M.D,
INSTRUCTOR IN CLINICAL MEDICINE IN THE UNIVERSITY OF MICHIGAN.

CASES of situs viscerum inversus have until recent years been discovered, studied, and reported chiefly by anatomists and pathologists. As a result of a correspondence with a large number of medical men of experience and prominence it would seem to me that the pendulum has swung about of late years, and that now a much larger percentage of these cases is discovered by the clinician. This fact is a natural result of the much more frequent and careful physical examinations that are now being made. However, even with this improvement, all physicians know that a very small percentage of even sick people submit to careful physical examination, and that the percentage of the entire population who are thus examined is extremely small.

Situs viscérum inversus is of great interest to the embryologist and anatomist. To the internist it presents very instructive problems in physical diagnosis.

Gruber made a remarkable collection of all cases found in the literature up to the year 1865. Of the seventy-nine cases which he reports only five or six were discovered during life. This fact seems rather remarkable, since his report covers more than two centuries. In 1643 Petrus Servius reported the first case as occurring at Rome.

Küchenmeister, up to the year 1888, collected 149 cases. The majority of these were discovered in the anatomical laboratory and on the post-mortem table. Pic, in 1895, increased the number of reported cases to 190.

Cases of partial situs inversus are not so common as those of complete transposition. Lochte, up to the year 1894, collected thirteen cases of this incomplete variety. In more than half very poor descriptions were given.

An attempt to collect all of the cases of situs viscerum inversus is extremely difficult and unsatisfactory, because they are reported in the literature under numerous headings. Perhaps something like 300 of these cases have been reported.

Since the spring of 1897 I have seen in hospital and private practice four cases of transposition of the viscera. It is a rather remarkable fact that three of these rare cases were seen within the short period of six months, an experience which I doubt being equalled even in the largest hospitals of the country. I am also familiar with three other cases of situs inversus discovered in the living subject by members of the internal medical staff, two by Dr. Warthin and one by Dr. Cowie.

The case which I saw first was with Dr. Chadbourne, in June, 1897, and has been reported by him and perhaps by a number of others, as he was a professional freak who went the rounds of medical schools exhibiting his anatomical abnormality for a compensation. This same patient, Schupfel by name, again presented himself at the hospital in July, 1902, and was demonstrated to my summer school section. He showed a complete transposition of the viscera, so far as could be demonstrated by clinical means. Inflation of the stomach and colon showed these viscera to be transposed. (Fig. 1.)

The three cases which I present in this article are bona fide patients —two farmers and a dental student—who learned for the first time of their peculiar abnormality.

My experience inclined me to believe that this condition was much more frequently detected in the living patient than one would infer from the literature. Acting upon this belief, nearly two years ago I sent letters to a number of prominent clinicians asking them the number of cases of congenital transposition of the viscera they had encountered in their work. Letters were also sent to a number of anatomists. The following interesting statements were received:

Dr. William Osler, Johns Hopkins: "Since the opening of the hospital we have seen, I should say, at least six cases."

Dr. Eshner, Philadelphia Polyclinic: "I beg to state that I cannot recall having seen a case of transposition of the viscera."

Dr. J. C. Wilson, Jefferson Medical College, Philadelphia: "I have encountered three demonstrable cases of transposition of the viscera, all adult males."

FIG. 1.

The upper curved line on the patient's right indicates the area of absolute cardiac dulness. The × just below this indicates the apex-beat. The curved line on the patient's right side indicates the splenic dulness. The straight line on the patient's left side indicates the upper border of the liver dulness; the small × indicates the lower border. The lowest curved line indicates the greater curvature of the stomach.

Dr. R. H. Fitz, Harvard Medical College: "I do not recall the number of living cases seen; I have no recollection of having examined after death a case of dextrocardia."

Dr. Warren Coleman, New York: "I do not recall having seen a case with transposition of the viscera."

Dr. I. N. Danforth, Chicago: "I never saw such a case in my life."

Dr. Allen Jones, Buffalo: "I have not seen a case of dextrocardia."

Dr. Frank Billings, Rush Medical College, Chicago: "I have seen

three cases of congenital transposition of the heart and abdominal viscera in my private and hospital work—one discovered in a babe about two weeks old, one in a young man between twenty and thirty years, and one in a man aged sixty-six years. The last suffered from gallstones, and was operated upon by Dr. Fenger, of Chicago. All three were unrecognized until the time when I first saw each case. Besides these three I have seen a case in a young man who travelled about exhibiting himself in medical schools."

Dr. John H. Musser, University of Pennsylvania, Philadelphia: "I have never seen any cases of congenital dextrocardia except those belonging to and reported by other physicians, as Dr. J. Dutton Steele and Dr. Joseph Sailer."

Dr. J. M. Anders, Medico-Chirurgical College, Philadelphia: "Three cases, but they have been seen while visiting various institutions here and elsewhere."

Dr. R. C. Cabot, Harvard Medical College: "I have seen two cases of transposition of the viscera. They were hospital cases in the service of Dr. Shattuck."

Dr. H. B. Newberry, Denver: "I have seen two cases—one a child, aged two or three years, also reported by Dr. J. A. Hall, and seen in consultation with him; a second in a young adult whom I was examining for life insurance. The abdominal viscera were displaced in both cases, as shown by the liver."

Dr. James Tyson, University of Pennsylvania, Philadelphia: "I recall only one well-remembered instance of transposition of the viscera occurring in my clinical experience. I remember seeing one other case years ago in a dissecting-room."

Dr. James Munson, Superintendent Michigan Insane Asylum at Traverse City: "While a member of the staff of the Pontiac (Michigan) Asylum I saw a case in which the diagnosis of complete transposition of the viscera was not made *intra vitam*, but at autopsy. During the last year of his life he had Addison's disease. I recollect that previous to his death the diagnosis of an enormously enlarged spleen had been made, and that the displacement of the heart had also been recognized; but my recollection is that it was thought to be due to dilatation."

Dr. Robert Preble, Chicago Medical College: "I have seen four cases of transposition of the viscera—three clinical, one post-mortem. Two of the clinical were stock cases in Vienna, the third is now a student at the Northwestern. In addition to these there is another case, in which the examination is incomplete, discovered while examining the heart for anæsthesia."

A Jacobi, College of Physicians and Surgeons, New York: "Only two that I remember."

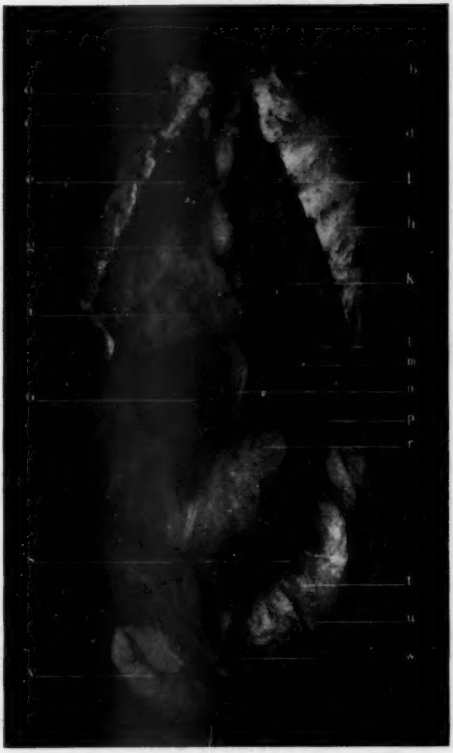
Dr. Atkinson, Baltimore: "Two cases of transposition of the viscera appearing at my clinic, and who travelled widely, exhibiting themselves."

Dr. C. G. Jennings, Detroit Medical College: "I have never met such a case."

Dr. I. W. Blackburn, National Hospital for the Insane, Washington, reported in the *Washington Medical Annals*, 1902, No. 2, vol. i., a very interesting case of transposition which came to autopsy. With his permission, an excellent photograph of this case is presented in this article. (Fig. 2.)

Dr. Naucrede, Ann Arbor: "One case, seen in the anatomical laboratory of the University of Pennsylvania, of which I helped to prepare a wax model. This case was reported by Dr. N. Hickman."

FIG. 2.



Transposition of viscera. Terms transposed in description: *a*. Right common carotid artery. *b*. Innominate vein. *c*. Left common carotid artery. *d*. Innominate artery. *e*. Left lung (?). *f*. Right lung (?). *g*. Pulmonary artery. *h*. Aorta. *i*. Right ventricle of heart. *k*. Appendix of right auricle. *l*. Diaphragm. *m*. Right lobe of liver. *n*. Suspensory ligament of liver. *o*. Left lobe of liver. *p*. Gall-bladder. *q*. Cardiac end of stomach and situation of spleen. *r*. Pyloric end of stomach. *s*. Gastrocolic omentum. *t*. Transverse colon dragged downward. *u*. Situation of cæcum. *v*. Sigmoid flexure. *w*. Omentum.

Dr. Irving Haynes, Professor of Anatomy, Cornell Medical College: "Although I have superintended the dissection of about 2500 subjects, I have never seen a case of transposition of the viscera."

Dr. Frederic H. Gerrish, Professor of Anatomy, Bowdoin Medical College, Portland, Me.: "I have never encountered a case of transposition of the viscera."

Dr. D. K. Shute, Washington, D.C.: "It has never been my good fortune to see any cases of transposition of the viscera."

Dr. S. Yutzy, Instructor in Anatomy, University of Michigan: "I have seen one case of transposition in ten years' service in the anatomical department. During this period about 750 subjects have been dissected. The case was a middle-aged man."

Members of the staffs at the four Michigan State Asylums inform me that the Pontiac case reported by Dr. Munson is the only case to be found on their records.

The above writers are all men of large experience.

Five well-known internists and four professors of anatomy replied that they had never seen a case of transposition.

Of the thirty-seven cases noted in the above letters all save six were discovered during life. In a few instances (travelling freaks) the same cases have probably been examined and reported by several of the writers. The majority, however, were discovered for the first time, and did not make a practice of exhibiting themselves.

In this country, at least, cases of transposition are nowadays much more frequently discovered during life than after death. Note the contrast between Gruber's report and my own. He collected seventy-nine cases, of which only five or six were discovered during life. In my collection, which simply covers the cases reported in the above letters, together with those with which I am personally familiar, there are forty-four cases, of which thirty-eight were discovered during life.

Report of Unpublished Cases.

CASE I.—Wm. B. consulted me June 13, 1900, complaining of symptoms of indigestion. He is a farmer, aged thirty-two years; is tall, slender, and poorly nourished. On examining his lungs by percussion tympany was encountered in the sixth intercostal space, right nipple line, there being no liver dulness. On the left side dulness is encountered on the sixth rib, nipple line, and eighth rib, mid-axillary line. Litten's phenomenon is present on both sides. Auscultation of both lungs shows good vesicular breathing.

Heart. I was much surprised to find the apex-beat in the fifth intercostal space one inch inside of the right nipple line, easily seen and felt after exercise.

Percussion shows tympany in the normal area for heart dulness. On the right side, however, there is an area of dulness encountered on the fifth rib, sternal line, and extending about one inch to the right; no dulness to the left.

Abdomen. Liver dulness encountered on the left side, nipple line, lower border of the sixth rib; extends down to the margin of the ribs in this line. In middle line, one-third of the distance from ensiform to navel. Just to the right of mid-line liver dulness merges with heart dulness. The liver is not felt.

Spleen. In the right mid-axillary line dulness is encountered at the upper border of the ninth rib, and extends down to the tenth inter-

costal space. It is about the size of a silver dollar. The spleen is not palpable.

Kidneys are not palpable.

Stomach was distended, but unsatisfactorily.

Testicles. Right hangs lower than the left.

CASE II.—A. G. S., dental student, aged twenty-one years, was sent to me by Director Fitzpatrick, of the gymnasium, who suspected some cardiac anomaly. There is no history of disease of the lungs, pleura, or heart. He was never a good distance runner because of shortness of breath. For years he has thought that his heart was on the right side, because he could feel it beating there. This patient is in good health, but does not look robust. Examination of lungs is negative.

Heart. Apex-beat is felt in the fifth intercostal space, just inside of the right nipple; dulness begins on the fourth rib, right sternal line, extends out to right parasternal line. There is no heart dulness on the left or under the sternum. Auscultation is negative except that at times the rhythm is somewhat irregular. The second sound in the right second intercostal space is louder than that in the left. The sounds are heard best to the right, but there are weak heart sounds heard in the location of normal apex-beat.

Abdomen. Liver dulness is encountered on the left side. Upper border, left sternal line, seventh costal cartilage; nipple line, seventh rib; mid-axillary line, eighth intercostal space. This dulness extends down to the margin of the ribs.

Spleen. In outlining the lower border of the right lung I was surprised to find no liver dulness. On percussing in the right mid-axillary line I found a small area of dulness beginning at the ninth rib, extending down about two inches and forward to the anterior axillary line.

Stomach was distended with acid and soda, showing a dislocation. The greater curvature is about three inches below the navel, lesser curvature one inch above. The fundus of the stomach seems to be on the right side, there being a broader area of distention here than on the left.

Colon was distended with air and filled first on the left side, extending about two inches above the navel. There was very little distention on the right side.

Testicles. Left hangs lower than the right.

Spinal Column. No curvature.

X-ray Examination. With the fluoroscope I obtained a good view of the heart beating to the right of the sternum.

CASE III.—I. C., merchant, aged sixty years, patient at the University Hospital. This patient had a chronic bronchitis and chronic rheumatism. He never suspected any dislocation of his organs. He is emaciated. Percussion and auscultation of the lungs reveal signs of emphysema and bronchitis, but of no condition which could have caused a dislocation of his heart to the right.

Heart. Apex-beat cannot be seen or felt on the left side, but in the fifth intercostal space, right side, nipple line, a faint pulsation is seen and felt.

Percussion. Along the left sternal line there is good resonance down to the sixth rib, where liver dulness is encountered. On the right side absolute heart dulness is encountered on the fourth rib, sternal line;

extends to the right, on a level with the fourth rib, to the parasternal line; with the fifth rib to within one inch of the nipple.

Auscultation. Over apex on the right side the sounds are strong; no murmurs are detected. In the second intercostal space, right, the second sound is much accentuated; in the second intercostal space, left, the second sound is very weak.

Abdomen. Unfortunately, a complete examination was not made.

CASE IV.—I am indebted to Dr. Cowie for the following report of this case. S., a travelling salesman, aged fifty years. His symptoms point to a chronic gastritis. An interesting point in his history is the fact that he was examined for life insurance five times without having this anomaly discovered. Examination of the lungs is negative.

Heart. Apex-beat not seen or felt in normal position. There is no dulness to the left of the sternum. Apex-beat is plainly seen and felt in the fifth intercostal space, just inside right nipple.

Auscultation shows heart sounds loudest to the right of the sternum.

Abdomen. In place of liver dulness in right hypochondrium there is a tympanitic note. In this region succussion sounds are brought out by deep palpation. In the left hypochondrium liver dulness is encountered—upper border of nipple line, seventh rib. This extends down to the margin of the ribs and far forward as the sternum.

Stomach. On distention with air it is seen to lie in the right hypochondrium, partially in the epigastrium, near the median line. It is not dislocated downward.

Kidneys are not palpable.

Testicles. The right much lower than the left. The genitals have a right-sided position with trousers on.

CASE V.—The notes on this case are very brief. Patient was colored, male, aged over twenty years; was examined in the out-patient department by Dr. Warthin. The condition of congenital dextrocardia was satisfactorily determined, but so much enthusiasm and interest were manifested in his case that he refused to return for a complete examination of the abdominal viscera, fearing that he was to be subjected to experimentation.

Acquired dextrocardia is a fairly common condition, resulting from contracting disease of the right lung or pleura, which pulls the heart over under the sternum, or even beyond. Again, it may be due to large collections of fluid (serous or purulent) in the left pleural cavity, which push the heart to varying degrees to the right. Inflammatory adhesions may fix the heart in this position, even after the cause has been removed by absorption or operation. A less common cause is the presence of a new-growth involving the left lung and pleura, or mediastinum.

A very striking case of this latter variety came under my observation last spring, in Dr. Dock's clinic. Fig. 3 well illustrates the conditions which were present.

The patient is a small woman, aged forty-five years. She is emaciated, weighing only ninety pounds. Three years ago she weighed about 115 pounds. On inspection of the thorax the left side is a trifle

fuller than the right. On deep breathing expansion is practically limited to the right side. Percussion shows absolute dulness over the entire left chest, front and back, except a very small area at the apex, which gives a tympanitic note. The dulness also extends across the sternum in front to the right parasternal line above the fourth rib, while below this it reaches almost to the nipple line. This dulness and the liver dulness are continuous. As the photograph well shows, resonance was obtained over only a very small part of the thorax in front. Behind, the right lung gives a hyperresonant note over its entire extent down to four fingers below the angle of the scapula. Litten's

FIG. 3.

O = apex-beat. The entire area between the dark lines was absolutely dull.

phenomenon is very distinct on the right, the shadow line moving from the eighth rib down three inches in the mid-axillary line. On the left side it is absent.

Auscultation. Over the dull area, front and axilla, breath sounds are practically absent; behind there is extremely weak vesicular breathing, perhaps conducted from the right side by the spinal column. Over the resonant area of the right lung there is exaggerated vesicular breathing.

The voice sounds are well transmitted over the right resonant area, while practically absent over the left dull area.

Vocal fremitus is very strong over right, but absent over the left chest.

Heart. Apex-beat is felt in the fourth intercostal space, nipple line, right side, most distinctly one inch inside of nipple line. There is also a distinct pulsation in the second and especially in the third intercostal space, right, extending almost to the nipple line.

Heart dulness is continuous with the large area of dulness to the left and below. It extends to within an inch of the right nipple, on a line with the fourth rib.

Auscultation. Over the dislocated apex the first and second sounds are moderately strong. The third intercostal space, right parasternal, first sound is murmurish; second sound is accentuated. Second intercostal space, left, sounds are weak. Pulse is small, of low tension, and regular.

After a consideration of these signs I concluded that there was an enormous collection of fluid in the left pleural cavity, which caused a dislocation of the heart to the right. A large exploratory needle was used twice by the medical interne, Dr. Pray, with no results beyond withdrawing a small amount of blood. Three days later I also used exploratory aspiration twice, but with negative results.

As a result of these findings I came to the conclusion that the cause of the dulness and dislocated organs was a new-growth involving the left pleura, lung, and perhaps the mediastinum.

Another possibility which must be considered is that of an old empyema, with greatly thickened pleura, and a large collection of thick, purulent material. However, it seems most likely that we would have been able to demonstrate pus had it been present.

A striking physical sign was the remarkable clubbing of the fingers, which is shown in the photograph.

The patient came to the hospital complaining of great weakness, a bad cough, and shortness of breath on exertion.

The present illness began four years ago with a cold. She was then troubled with shortness of breath on bending over, with pains in the left side and shoulder. The cough has become much more troublesome during the past two or three years. It has always been dry until a few weeks ago, when the patient caught cold; since then she has raised some sputum. During the past few weeks she has had very little pain in the left side, but there is a feeling as if the lungs were compressed.

During the patient's stay in the hospital her temperature has seldom reached 100° F. She came to the hospital with the diagnosis of consumption. Examination of the sputum for tubercle bacilli while here was always negative. This patient died in January, 1902. Her attending physician, Dr. Fay, of Carlton, Mich., writes me that autopsy revealed an enormous mediastinal tumor, about the shape and size of a medium-sized watermelon.

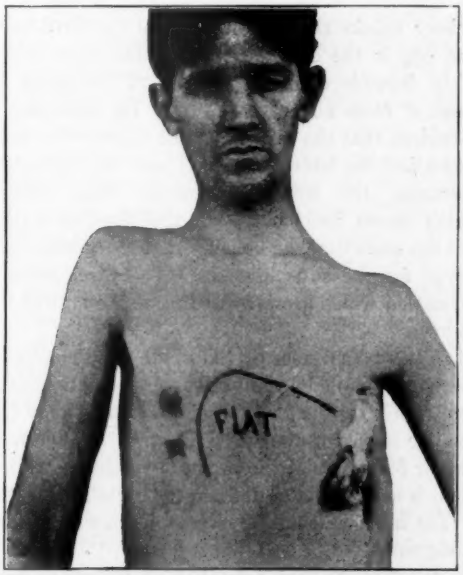
Another striking case of acquired dextrocardia is well illustrated by Fig. 4. The change in the position of the heart is secondary to an empyema of the left chest of long standing, with extreme retraction of the entire left side. The left side of the chest, with the exception of the apex, does not expand at all. The right side expands fairly well.

Heart. Forcible pulsation is seen to the right of the sternum, in the second, third, fourth, and fifth intercostal spaces; strongest in the fourth. The apex-beat is in the fifth intercostal space, nipple line.

Auscultation. At the apex both first and second sounds are loud and clear-cut. In the second intercostal space, right, the second sound is accentuated. In the second intercostal space, left, both first and second sounds are murmurish. In this area splashing sounds could be heard with each pulsation of the heart during forced inspiration, due in all probability to the sudden movement of the purulent fluid and air in the empyemic cavity (open pneumothorax).

The patient was taken sick in December, 1900. Two months later he noticed the heart beating on the right side, in about the same position which it occupies at present. In December, 1901, Dr. Nancrede resected six ribs. Marked retraction of the left chest followed, but the position of the heart was not altered by the operation.

FIG. 4.



× = areas of cardiac pulsation.

Theories Explaining the Development of Congenital Transposition of the Viscera. These are chiefly of interest to the embryologist and anatomist, and will hardly be understood except by those who have devoted special study to embryology. The following are some of them:

Von Baer explains transposition by the turning of the embryo in the opposite direction—that is, the embryo normally lies on the left

side of the umbilical vesicle; but if it lies on the right side, then we have transposition. According to him, this occurs at the beginning of the developmental period.

Förster considers situs inversus a malformation in which the transposition of the anlagen takes place in the first embryonal formation. In the double monster the fœtus of the right side shows a complete transposition, while the fœtus on the left side shows a normal situs.

Rindfleisch believes that the spiral turning of the blood column is responsible for the displacement of the heart. Normally it flows from left to right, but in situs inversus an opposite direction must obtain. The asymmetry of the heart is made responsible for all asymmetry in the animal body.

Virchow emphasizes the influence of the umbilical cord. In situs inversus it is wound spirally to the right; in the situs solitus to the left.

Küchenmeister thinks that the location of the fertilized disk at the surface of the egg is the essential thing. The normal situs in single birth probably depends upon the growth of the germ from below upward instead of from above downward. He says that from this it must be self-evident that the turning of the embryo has been inverted. This must also affect the later spleen side and the side of the arterial heart. Concerning the congenital partial situs viscerum—solito inversus—which shows itself either in the chest or belly, but not in both places at the same time, he believes that the growth, on the whole, follows the type for the situs inversus. The rarer partial situs is an inhibition formation which grows according to the type of the normally projected embryo.

Martinotti in the transversus of the single born emphasizes the condition of the vena omphalomesenterica, first mentioned by Dareste. The direction which the heart loop takes depends upon the dissimilar growth of the two halves of the vascular area. Under normal conditions a dissimilar formation of the two halves exists. The left omphalomesenteric vein is more developed than the right; the right gradually disappears. The heart reacts in a very sensitive way toward the cause of situs transversus.

Marchand says that the loop formation of the venæ omphalomesenterica about the intestines under normal conditions prevents the intestines from slipping toward the right; so a right turning takes place if the loop formation is absent. He considers the left-sided persistent vena omphalomesenterica the cause of the right position of the stomach. In a more recent article Marchand does not believe that the development of the vena omphalomesenterica can have an influence upon the rotation of the stomach.

Lochte advances the view that the growth of the organ, considered in the sense of situs solitus, is associated with a persistence of left-sided omphalomesenterica and umbilical veins, while those of situs transversus totalis, on the other hand, are associated with corresponding right-sided veins.

To the clinician, transposition of the viscera presents many interesting problems in differential diagnosis. The displacement of the heart to the right makes it necessary to examine the lungs and pleura carefully in order to exclude acquired displacements. The discovery of an enlarged area of dulness in the left hypochondrium suggests a number of possibilities. It is most likely an enlarged spleen, either of leukæmia, malaria, splenomegaly, etc. This point is illustrated by actual cases in practice. In Munson's case, referred to above, the diagnosis of an enormously enlarged spleen had been made, and the displacement of the heart was thought to be due to dilatation.

In the normal patient it is a very common experience to find an entire absence of liver dulness in the right hypochondrium. It is also common to find the apex-beat neither seen nor felt on the left side, especially if the patient is quiet and in the horizontal position. Heart dulness is also frequently absent. So it is easy to understand how these cases of transposition are often overlooked.

It is possible to mistake an aneurism of the arch for a dislocated heart. This fact was recently brought to my attention.

Gruber refers to the following errors in diagnosis: In one case of transposition a pain in the right hypochondrium led to the diagnosis of a chronic inflammation of the liver. In another case a soldier was wounded in a duel in the right hypochondrium; from the position of the wound and the vomiting of green fluid it was thought that the liver had been penetrated. In a third case in the Würzburg clinic the transposed liver was diagnosed as a splenic tumor. In a fourth case—one of a cancer of the pylorus in a transposed stomach—the hard tumor felt deep in the left hypochondrium, and was thought to belong to the stomach or the pancreas.

Gruber arrived at a number of interesting conclusions from a study of 79 cases. Concerning the sex, there were 49 men, 19 women, and 11 in which sex was not mentioned. These individuals lived as long as those with normally placed organs; 5 of the 19 women lived to an age between 70 and 84 years. The women were normally fruitful; one gave birth to twelve children. Among the 79, 4 died an unnatural death, and only 4 were extremely malformed. There was transposition of both chest and abdominal organs in 71; of the abdominal organs alone in 8. In the first kind the transposition was complete, in the latter incomplete. Lungs were transposed in 35 of 71 cases;

the right had two lobes and the left three. In 2 cases they were not transposed; in 2 both lungs had two lobes; in 1 the right had one lobe and the left 2 lobes. Spine: curvature of the dorsal portion is mentioned in only 11 cases. In 7 of these it was to the left; in four to the right, as normally. We cannot draw the conclusion that persons with transposition are more likely to be left-handed than those with normally located viscera. The position of the testicle was mentioned only 7 times. In 4 the right was lower; in 1 the left; in 1 the left had not descended. The lower position of the right testicle is unimportant as a sign of situs inversus. In only 9 cases were there notes on the position of the kidneys. In 7 the left was lower, in 2 the right. In 32 cases in which the vessels arising from the arch of the aorta are mentioned these were transposed 29 to 30 times.

H. Steinhaüser mentions the fact that in the operation of œsophagotomy it is well to know that the œsophagus lies over the right trachea in persons with transposition.

In situs partialis the transposition of the abdominal organs may be very irregular. In one case the stomach and duodenum were normally located, while the other organs were transposed. In another case the liver alone was transposed.

In 1888 a case of pure dextrocardia, with congenital pulmonary stenosis, without malposition of the viscera in general, was shown to the Vienna Medical Society by Dr. Gruss. In discussing the case, Von Bamberger concurred in the diagnosis, and remarked that Professor Schrötter had lately stated that no single case of pure dextrocardia had ever been proved; whereas all anatomists of experience—for example, Rokitansky, Friedberg, Förster, etc.—had mentioned such cases, and he himself had seen two.

The above quotation emphasizes the fact that partial situs is a much rarer condition than complete. If the transposition is located in the abdominal cavity it will most likely be overlooked in the physical examination.

REVIEWS.

LECTURES ON THE HISTORY OF PHYSIOLOGY. By SIR MICHAEL FOSTER, M.P., M.D., Professor of Physiology in the University of Cambridge. The Macmillan Company, 1901.

FOR the "Lane Lectures" at the Cooper Medical College, San Francisco, for 1900, Sir Michael Foster most happily chose the history of physiology during the sixteenth, seventeenth, and eighteenth centuries. In many ways, for many good deeds, the profession is indebted to Michael Foster. His text-book has taught both teachers and students; to him more than to any one man is due the rise of the new school of physiology in England, while largely as a result of his efforts the university which can boast of Caius, Harvey, and Glisson has a first-class medical school.

These lectures form a contribution to medical literature of the highest order. The style is so charmingly lucid, and Sir Michael has such a power of seizing the salient points in a story, and has given such a human interest to the tale, that the work is destined to be a classic in the history of medicine. There has been nothing of the same kind in our literature, and the title could have been just as well the history of scientific medicine during these centuries. It is a work which cannot be too widely known; teachers should read it carefully, and should recommend it to their senior students, who will find in these stories of the heroes of medicine just the right kind of instruction.

The book opens with an account of Vesalius, the founder of modern anatomy, the story of whose life has often been told, but never by a more sympathetic writer. The essential feature of his work is thus told in a paragraph: "The 'new birth' of the fifteenth and sixteenth centuries was in essence a revolt against authority as the guide in knowledge; and the work of Andreas Vesalius, of which I am speaking, marks an epoch, since by it the idol of authority in anatomical science was shattered to pieces, never to be put together again. Vesalius describes the structure of the human body such as he found it to be by actual examination, by appealing to dissection, by looking at things as they are. He dared not only to show how often Galen was wrong, but to insist that when Galen was right he was to be followed, not because he had said it, but because what he said was in accordance with what anyone who took the pains to inquire could assure himself to be the real state of things."

When one examines the *De Fabrica*, with its accurate plates and beautiful letter-press, it is hard to believe that this was the work of a young man not yet thirty. Vesalius had a high and imperious spirit, and the bigoted opposition which his great work aroused, even in his friends, entered like iron into his soul. "If the work on which he had

labored so long, and which he felt to be so full of promise, met with such a reception, why should he continue to labor? Why should he go on casting his pearls before swine? He had by him manuscripts of various kinds the embodiment of observations and thoughts not included in the *Fabrica*. What they were we can only guess; what the world lost in their loss we shall never know. In a fit of passion he burnt them all, and the Emperor Charles V. offering him the post of court physician, he shook from his feet, in 1544, the dust of the city in whose university he had done so much, and still a youth, who had not yet attained the thirties, ended a career of science so gloriously begun."

Vesalius was the first modern anatomist. Harvey was the first modern physiologist. As one reads the *Exercitatio de Cordis Motu* to-day there is a feeling that the author approaches his problems in a truly scientific spirit, and there is nothing in the work which jars or which suggests mediævalism. Harvey demonstrated the circulation of the blood. Vesalius, Servetus, and Fabricius led up to Harvey, and the author gives due credit to the work of Columbus and Servetus; but Harvey took up the experimental method used by Galen and by the Alexandrian physicians, and demonstrated in a way that the simplest could follow, the complete circulation of the blood. It is not necessary to dwell on this well-known chapter further than to call attention to the fairness and the clearness with which the history of this great discovery is presented.

One of the most interesting lectures (III.) is that on the "Influence on Medicine of the New Science of Physics." In his treatise on *Man*, Descartes, whom Foster calls the Herbert Spencer of the age, maintained the theory that man was an earthly machine governed by a rational soul, and attempted to apply to the interpretation of the phenomena of living beings the philosophy of exact mathematics and physics. The lecture is largely devoted to the life and work of a remarkable man, never before introduced so fully or so ably to an English reading audience—Borelli, mathematician, physician, astronomer, and physicist. Born in 1608, he came under the influence of Galileo, and in 1656 was elected to the chair of mathematics at Pisa, where he had as colleagues Malpighi and Redi. Borelli was the first to apply the exact mathematical and physical knowledge which had grown so greatly in explanation of the problems of the living body. In his great work *De Motu Animalium*, "he treats in succession of the various problems of muscular mechanics, of flexion and of extension, and of the more complex problems of standing, walking, running, and other forms of locomotion; he investigated these in the same rigid, exact manner, calling in the aid of mathematical figures and calculations, as he and others had investigated the problems of falling bodies, and of the action of various propulsive and other machines."

He discusses the mechanism of the circulation of the blood, of the action of the heart, and his work is really the foundation of all our knowledge of animal mechanics. "When we consider the effect which a perusal of Borelli's book has upon the reader now, we can easily understand how he was a founder of a great school which flourished long after him. He was so successful in his mechanical solutions of physiological problems that many coming after him readily rushed to the conclusion that all such problems could be solved by the same methods; and, as is often the case, the less qualified, alike as regards mechanical as

well as physiological knowledge and insight, to follow in Borelli's path, were the men of succeeding times the more loudly did they often proclaim the might of Borelli's method. Thus there came in the times after Borelli a school who, imitating and often mimicking Borelli, proposed to explain all physiological phenomena by the help of mathematical formulæ, and of hypotheses concerning forces and the shapes and sizes of particles, the iatro-mathematical or iatro-physical school."

The structure of muscle was first clearly demonstrated by Nicholas Stensen, a Dane, whose Latin name, Steno, is given to the duct which he discovered. His romantic story matches almost that of Vesalius. After publishing, in 1662, his *Observationes Anatomicæ*, while as yet a young man of twenty-four years, he seems to have wandered about, teaching here and there, and in 1666 he became court physician to Ferdinand II. at Florence. He worked at comparative anatomy and geology, to which science he made an important contribution. In 1672 he returned for a time to Copenhagen, but two years later he was again in Florence. Then, while still a young man of thirty-six summers, came a sudden and profound change. In Paris he had come under the influence of the great Bossuet, and, though brought up a staunch Protestant, the seed had fallen on a good soil. "One day, visiting at Florence the pharmacy attached to the Sancta Maria Novello (the same pharmacy at which to-day you may buy orris root and other preparations), in order to buy some drug, the holy brother who sold him the medicine dropped some words about the remedies for the soul. The stray arrow entered between the joints of the harness. New thoughts were stirred in the mind of the man of science and of the world, and within a year, to the astonishment of his friends and the dismay of all the friends of the new learning, he forsook all his old studies, gave up all inquiry into the works of nature, and, taking orders, solemnly devoted himself henceforth to the works of God and religion." Made subsequently a Roman Catholic Bishop, he for a time resumed his old work as Professor of Anatomy in the University of Copenhagen, but "he soon gave up all attempts to work his old life into his new calling." He devoted himself to the usual duties of a priest, and, at Schwerin, lived a life of severe self-denial, laboring constantly for the welfare of the poor. "The privations which he laid upon himself and the toils which he underwent for others were too much for the body which had once filled so much of his thoughts, and which he now held as a thing of naught. He wore himself to death, and died in 1686, at the relatively early age of forty-eight."

The invention of the microscope revolutionized the study of anatomy in the seventeenth century, and the labors of Malpighi, Leeuwenhoek, Swammerdam, and Hooke founded the new science of histology. Malpighi was the strong man of the period, and the pen-picture of the great histologist is drawn with singular felicity. Take the contrast between two friends: "Borelli, twenty years older than Malpighi, self-asserting, confident, claiming as his own not only what he had done, but at times what had been done by others; angry if his own merits were not fully acknowledged, impatient of the praises of others, bore himself, as we have said, in daily life with a taciturn coldness if not with a rough fretfulness which kept many who admired his talents from looking upon him as a friend. Malpighi, kindly even to softness, ready to give his affections to those who seemed drawn to him, devoted wholly to those who had won his love, modest and retiring even to timidity, bold only in the

interests of truth and right, never in his own, lived a life such as the sweet, delicate outlines of his face bespoke; beloved for the sake of himself, even by those who were not competent to judge of his talents and his work." Malpighi was a great biologist, and his researches in embryology, comparative anatomy, and vegetable morphology were characterized, as Foster says, by the light of genius and by the deepest philosophic insight. He completed the link in Harvey's demonstration by discovering the capillary circulation. He described the vesicular structure of the lungs, and gave the first scientific account of the finer anatomy of the liver, pancreas, spleen, and kidneys. A professor of medicine, a busy practitioner, an ardent investigator, yet of delicate habit of body, Malpighi illustrates as well as anyone in the history of science how much may be accomplished by a man who has what Donne calls "the sacred hunger of science."

"The Rise of Chemical Physiology," the subject of Lecture V., introduces us to the alchemist, Basil Valentine, and his three elements; to Paracelsus, the first great pharmacologist, the leader of the revolt against Galenic practice; and particularly to Van Helmont, one of the founders of modern chemistry, a careful, exact student, who is remembered by his *Archæus*, and whose doctrine of fermentation influences medical opinion at the present day.

The chemistry of digestion, as studied by Sylvius and his pupils, carries us on to a more modern stage and to the conception of the identity of the chemical processes in dead and living things. De Graaf, Stensen, Peyer, von Brunner (names on our lips daily) helped to clear the mysteries of intestinal digestion, and the salient features of the work of each are presented in a most attractive way. Here, again, it is simply delightful to have the dry bones of old and long-forgotten views live again by the personal interest we are compelled to take in the men who announced them.

The physiology of respiration, to which Borelli has made such important contributions, was worked out largely by a group of English physiologists of the seventeenth century. Boyle, Hooke, Lower, and Mayow were worthy children of the great Harvey. The story of Mayow and his remarkable contributions to the physiology of respiration will be read with exceptional interest by teachers, to a majority of whom, as to the writer, there will be the added interest of novelty. His work, with certain changes in phraseology, could be incorporated in a modern textbook. At a time when the men of chemistry were battling with the spiritualistic fermentations of Van Helmont and the material effervescences of Sylvius, Mayow, by a series of brilliant experiments, had grasped the essential truths of the subject. "He saw that the nitro-aërial particles of the air, or oxygen, as we would say, formed only a part of the atmosphere; that it was essential for burning; that it was essential for all the chemical changes on which life depends; that it was absorbed into the blood from the lungs, carried by the blood to the tissues, and in the tissues was the pivot, the essential factor of the chemical changes by which the vital activities of this or that tissue are manifested. It was essential in muscle to the occurrence of muscular contractions; it was essential in the brain to the development of animal spirits."

In Lecture VIII., which deals with the physiology of digestion in the eighteenth century, we have graphic pictures of Boerhaave and his great pupil, Haller, and of Reaumur and of Spallanzani.

Mayow's seed of truth fell on uncongenial soil, and, as Foster says, the world had to await for more than one hundred years until his thoughts arose, as it were, from the grave in a new dress and with a new name. The modern doctrines of respiration (Lecture IX.) date from the researches of Black, Priestley, and Lavoisier. The story of phlogiston, and of the discovery of oxygen, of carbon dioxide, and of nitrogen is skilfully drawn. Here, again, the human interest absorbs our attention, and the sad fate of the brilliant Lavoisier haunts the memory. "On the morning of May 9, 1794, there passed in carts from the Conciergerie to the Place de la Révolution a procession of men to meet their death. As the sharp stroke of the guillotine severed in turn the neck of the fourth of these, there passed away from this world, in his fifty-first year, this master mind of science, who had done so much to draw aside from truth the veil of man's ignorance and wrong thought; and there passed away, too, the hope of his drawing aside yet other folds of that veil—folds which perhaps wrap us round even to-day."

The concluding lecture is upon the older doctrine of the nervous system. The visionary reasoning of Descartes and of Willis are well contrasted with the sensible moderate views of Vesalius and of Stensen. For the first time, so far as I remember, justice has been done by an Englishman to Glisson, and to his position as the founder of the doctrine of irritability of tissues. Virchow has repeatedly referred in addresses to Glisson's great merit in this matter, and it is pleasant to see his views clearly set forth by the author. Physiologists will read with interest of Glisson's early plethysmographic experiment demonstrating the shrinkage of muscle during contraction.

In this much too brief outline we have endeavored to show the human interest with which the author has clothed these admirable lectures. The story of such men as Vesalius, Harvey, Malpighi, Borelli, Stensen, Mayow, Lower, Lavoisier, and others, with their love of truth and their capacity for patient, honest work, should be in the hands of every student of medicine. As the stream of knowledge grows more rapid, we teachers live too much—we have to, I suppose—in the swift current, and few of us have time, too few the inclination, to go up stream to the sources of our art and science, and yet there is not a question which comes before us which cannot be most safely approached from the historical side. Even when time and opportunity are lacking for personal investigation, as they often must be to busy teachers, the attitude of mind counts for much, and this work will, I am sure, help many of us to a proper appreciation of the great masters of medicine. W. O.

A TEXT-BOOK OF THE PRACTICE OF MEDICINE. By JAMES M. ANDERS, M.D., Ph.D., LL.D., Professor of the Practice of Medicine and of Clinical Medicine in the Medico-Chirurgical College, Philadelphia; Attending Physician to the Medico-Chirurgical College and Samaritan Hospitals of Philadelphia, etc. Fourth edition, thoroughly revised. Philadelphia and London: Wm. B. Saunders & Co.

THE rapid exhaustion of the various editions of this work, making a fifth necessary within a period of four years, speaks eloquently for its popularity. Few authors are so highly complimented. But this marked

popularity is not without its drawbacks to both the author and the reader. It does not give the former time to carefully revise his work, while it results for the latter in the production of a work of less merit. In the present edition, however, the author has succeeded in making quite a number of valuable additions, especially along the line of recent developments, and in carefully rewriting the articles to which the most extensive additions have been made. In so doing he has aimed at the elimination of all superfluous words and sentences, and by thus securing greater conciseness of expression he has succeeded in adding extensively to the articles on Typhoid Fever and Variola without increasing the number of pages. This same slashing process applied to the remaining chapters would result in making the book much more readable. Many of the articles have been more or less changed.

In the chapter on Yellow Fever are given the most recent views on its bacteriology and modes of infection, especial reference being made to the recent extensive studies of Reed. The adoption of the latter's views has necessitated changes in the paragraphs relating to prophylaxis and quarantine. It would scarcely seem advisable, however, until these researches are more widely confirmed, to do away entirely with quarantine methods, as is recommended. The recent advances in the serum therapy of yellow fever are noted. The paragraph on the bacteriology of cerebro-spinal meningitis has been modified in accordance with the most recent investigations, and a paragraph on Kernig's sign, more fully describing its cause and method of elicitation, has been added. The description of lumbar puncture has been changed, and this procedure and laminectomy have been included among the remedial agents recommended.

The changes introduced contain some striking alterations of ideas, doubtless the result of more extended experience. Thus, in the article on Neurasthenia in the fourth edition, it is written under the heading of Symptoms: "The subjective symptoms are protean and varied, but these are often learned after close interrogation, the patient being unduly reticent as a rule;" in the present edition, under the same heading, the following appears: "The subjective symptoms are protean and varied, and are usually described with great detail, for the patients are, as a rule, exceedingly voluble." The classification of diseases used in the former editions have been retained in this. The chief objection to it is the arrangement of muscular rheumatism, chronic articular rheumatism, Weil's disease, Malta fever, febricula, milk sickness, miliary fever, foot and mouth disease, and glandular fever, under the heading, "Infectious Diseases of Unknown Etiology." In the first place, the infectious nature of some of these conditions is improbable; and, in the second place, one would infer from finding such diseases as variola, syphilis, parotitis, etc., in the preceding chapter, under the heading Infectious Diseases, that the etiology of these conditions is definitely known.

The book contains many excellent chapters, especially those devoted to descriptions of the infectious diseases and to the diseases of the nervous system. As a text-book for students it is too comprehensive; that is, it contains entirely too much material which is purely speculative, of no use to the student, and only tends to confuse his mind, which is already overburdened with essential facts. It must serve a useful purpose as a book of reference, since it presents in a readable manner the results of most of the work of value that has been done in recent years. S. M. H.

THE PRACTICAL MEDICINE SERIES OF YEAR BOOKS, COMPRISING TEN VOLUMES ON THE YEAR'S PROGRESS IN MEDICINE AND SURGERY. Issued monthly. Under the general editorial charge of GUSTAVUS P. HEAD, M.D., Professor of Laryngology and Rhinology, Chicago Post-Graduate Medical School. Vol. I., General Medicine. Edited by FRANK BILLINGS, M.S., M.D., Head of Medical Department and Dean of the Faculty of Rush Medical College, Chicago, with the collaboration of S. C. STANTON, M.D. Pp. 270. Chicago: The Year Book Publishers, 40 Dearborn Street.

THE editors of this volume have made a readable book, covering part of the ground of general medicine from January to October, 1901, giving summaries of many important articles, in the choice of which their judgment has been good in the main. The abstracts are written in a smooth and even style, which, with the orderly arrangement and the small size of the book, makes the reading of it easy and pleasant.

The plan of the publishers is to issue a volume monthly for ten months of the year, different subjects being assigned to each volume. This makes a certain unevenness in covering the ground which appears detrimental. Thus, consideration of the diseases of the alimentary tract, and allied organs and the summer diseases are postponed until May, 1902. A. H.

THE ROLLER BANDAGE. By WM. BARTON HOPKINS, Surgeon to Pennsylvania Hospital and to the Orthopædic Hospital and Infirmary for Nervous Diseases. Fifth edition, revised. Philadelphia: J. B. Lippincott Company, 1902.

IN this little book is condensed the vast experience of its author as a teacher and as a surgeon to a hospital with one of the largest accident services in this country. The book has already won for itself a most enviable reputation, and for many years has been used as a standard in the branch whereof it treats. The fifth edition is materially changed, the plates and electrotypes of the former editions having been destroyed by fire, consequently rendering necessary the rewriting and reproduction of the letter-press and pictures.

The book should really be considered as an exposition of the principles of bandaging, accompanied by illustrations which show the proper way of practising the art. The text is noticeable for its extreme conciseness and lucidity; there is not an unnecessary word to be found throughout. This brevity is rendered possible by the truly remarkable illustrations which accompany the text. These are not only artistic, but they have been adopted by the author with a skill akin to genius to the exigencies of the case. Although the illustrations are most profuse, we have been unable to find a single one which could be considered as inserted for the purpose of padding. A glance at any of those which are used for illustrations of the method of applying any particular bandage is sufficient to show the way of application in such a manner that the student cannot fail to grasp the idea. The author has evidently so familiarized himself with the needs of students and, it might be added,

of practitioners of medicine, for this book may be well used to advantage by many a man who has long since possessed a diploma, that his book is admirably adapted to meet their requirements.

Dr. Hopkins' book may be regarded as the standard work on the roller bandage in this country. For many years it has held a pre-eminent position, and, though previous editions have seemed incapable of improvement, the present edition has demonstrated that it has been possible for the author to surpass even his former efforts. F. R. P.

A Manual of Otology. By Gorham Bacon, A.B., M.D., Professor of Otology in Cornell University Medical College, N. Y.; Aural Surgeon New York Eye and Ear Infirmary. With an Introductory Chapter by Clarence John Blake, M.D., Professor of Otology in Harvard University. Third edition, revised and enlarged, with 120 illustrations and 7 plates. Philadelphia and New York: Lea Brothers & Co.

The previous editions of this manual have been so recently reviewed at length in these columns, and the book has assumed such an assured position as a standard authority, and is so familiar to all teachers and students of the subject, that an extended notice is hardly required at the present time. Suffice it to say that the chief changes made in the present revision consist in additions to the already large number of illustrations and a consideration of lumbar puncture and the significance of leucocytosis.

Dr. Bacon's book fulfils its purpose in every respect. It well deserves to be called the standard manual of otology in the English language. The author's concise yet lucid style has enabled him to present within its limits an epitome of aural surgery comprising all the essentials of that art. The book is a model for all works of a similar nature. It has been universally adopted by teachers, and is deservedly popular with students and general practitioners who desire a readily comprehensible presentation of the subject of which it treats.

The author has been particularly happy in his choice of illustrations to accompany the text. While generous in number, there is not one which does not elucidate and add to the value of the letter-press.

F. R. P.

Mother and Child. By Edward P. Davis, A.M., M.D., Professor of Obstetrics in the Jefferson Medical College; Professor of Obstetrics and Diseases of Infancy in the Philadelphia Polyclinic; Visiting Obstetrician to the Jefferson, Phi'adelphia, and Polyclinic Hospitals, etc. Second edition. Philadelphia: J. B. Lippincott Company, 1902.

We know of no book which could better be placed in the hands of the prospective mother. One of our reasons for the above statement is that it does not attempt the rôle of the family physician, but simply aims to supply information which every intelligent mother should know, thus lightening the work of the doctor, and also rendering his orders

more intelligible. There is a most gratifying avoidance of all pathological and anatomical data, and even a description of the female generative organs is omitted, for which lack of completeness we are very thankful.

On the other hand, the book contains full and complete directions upon all subjects relative to the care of the mother and child, even including chapters upon emergencies, contagious diseases, and the proper use of external applications. A very satisfactory appendix, giving the method of preparation of various articles of diet suitable for the young child, is included. The text is very acceptably illustrated by a number of pictures which the feminine mind cannot but consider charming. Of special value are the portions of the book devoted to the feeding and clothing of the infant. W. R. N.

SUNSTROKE DURING MARCHES, WITH STATISTICS FROM THE ACTS OF THE MEDICAL DIVISION OF THE PRUSSIAN MINISTRY OF WAR. By DR A. HILLER, Chief Staff Physician. With 6 wood-cuts and 3 charts. Berlin: August Hirschwald, 1902.

THE main portion of the book is based upon the records of sunstroke cases occurring in the Prussian army. Taking this mass of material as a basis, the author has added many series of cases collected from literature, beside experimental researches, and has formed out of the whole a most complete and interesting monograph upon the subject. No important new facts are added, but as a compilation the book accomplishes its purpose. All the important phases of the subject are considered in some detail, but owing to the fact that the author views the subject from a military standpoint, much space is given to discussions of the predisposing factors of sunstroke, and especially to the part played in this connection by improper clothing and physical exhaustion. The chapter devoted to the clinical description of the affection is complete, and embraces a summary of the complications and sequelæ following sunstroke. That portion of the book allotted to the pathology of the disease is likewise good, and various observations made upon the pathological changes in the blood of these cases are brought together for the first time. Practically no new methods of treatment are suggested, but statistics of the results of those therapeutic measures most in use are given in full. W. T. L.

THE ROENTGEN RAYS IN MEDICINE AND SURGERY AS AN AID IN DIAGNOSIS AND AS A THERAPEUTIC AGENT. By FRANCIS H. WILLIAMS, M.D. Second edition, with 410 illustrations and enlarged appendix. New York and London: The Macmillan Co., 1902.

THE second edition of this book has few new features, the chief addition upon the subject of radiotherapy being placed in the appendix. The therapeutic uses of the X-ray have become so numerous and remarkable that only a book revised every few months can be kept abreast with the times.

The results obtained and the methods used in the treatment of various diseases, both by the author and by others, are fully but concisely stated, being briefly illustrated with reports of cases. The surgical uses of the X-ray in the diagnosis of fractures, dislocations, and the detection of foreign bodies are well demonstrated.

Too little attention has been given to the subject of X-ray photography, since we must depend in great part upon photography for records and for accurate diagnosis. The author seems to be impressed with the idea that this information can be got best by experience. Experience would also give the other information needed, but would be slow and expensive.

The diagnosis of thoracic lesions is most ably described and illustrated. The author points out the importance of the use of the X-ray in diagnosing affections of the chest, and calls attention to the most common mistakes that may be made in the interpretation of the shadows. The author has not yet recognized the value of the X-ray in the diagnosis of brain lesions, and dismisses the subject with a short paragraph. Abdominal lesions have, however, been given their due share of attention.

The author's general experience and his recognition of the needs of the clinician are shown throughout the work. As a whole, it is a valuable addition to the literature upon the subject, and can be recommended both to the practitioner and to the student. The fact that the first edition was exhausted in three months' time is evidence that the book meets a popular demand. G. E. P.

ÉTUDES SUR LA TUBERCULOSE ET SON TRAITEMENT. Par LE DOCTEUR G. P. COROMILAS. Paris: A. Maloine, editeur, 1902.

FOR upward of fourteen years Coromilas has been treating tuberculosis in its various forms with sulphite of carbon (sulfure de carbone.) This compilation of several memoirs deals in turn with the various forms of tuberculosis, and is divided into five general parts, dealing successively with tuberculous coxalgia (osteo-arthritis), tuberculous arthritis, complicated and doubtful cases of tuberculosis, pulmonary tuberculosis, and finally intestinal tuberculosis.

In cases of coxalgia the general tuberculous diathesis should be treated with syrup of sulphite of carbon, and the local lesions by immobilization and injections of carbon sulphite into the focus of disease.

Cases of tuberculous arthritis are treated in the same way by local injections, and the sulphite of carbon is found to be strongly bactericidal, to facilitate the breaking down of tuberculous areas, and finally to aid in the restoration of the part to a healthy condition.

The results claimed for the treatment of pulmonary tuberculosis are even more remarkable. The sulphite of carbon mixed with olive oil or turpentine is used for inhalation or direct injection into tuberculous cavities, and it is found to be non-toxic, to neutralize the virulence of the tubercle bacillus, to dissolve and cicatrize small tubercles, and to contract large ones. Intestinal tuberculosis and tuberculous peritonitis are treated by small doses per os and lavage.

In spite of the astounding efficacy of his panacea, the author does not fail to mention the value of feeding, fresh air, and rest as additional factors in the cure. F. P. G.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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The Treatment of Diabetes Mellitus and Its Complications by the Use of a Diet Containing Potatoes.—Mossé (*Revue de Médecine*, 1902, pp. 107, 278, 371, and 621) in a series of articles deals with his experiences in the use of potatoes in the treatment of diabetes mellitus. He starts out with the statement that the object sought for in the treatment of diabetes mellitus is the prevention or reduction of the hyperglycæmia. This may be brought about either by stimulating organic combustion, and thus hastening the destruction of the grape sugar, or by suppressing from the diet or reducing to a strict minimum the sugars and carbohydrates convertible into glucose.

Mossé says that potatoes are generally held to be *injurious* in diabetes, and are usually placed in the list of forbidden articles. He believes, on the contrary, that they are not only *permissible*, but even *useful*. Potatoes may, with advantage to the patient, be given in substitution for wheat bread in the proportion of 2.5 to 3 of the former (weighed raw) to one of the latter. In his dietetic experiments he allowed his diabetic patients to have the enormous amount of 1 to 1.5 kilogrammes of potatoes (weighed raw) daily. In some instances the amount was increased up to 3 kilogrammes, or about six pounds. Wheat bread contains from 47 to 55 per cent. of starch, whereas fresh potatoes contain from 16 to 24 per cent., or an average of 20. The potatoes may be given in various ways, but in all his cases Mossé had them baked. In his experiments usually from 1 to 1.5 kilos of potatoes were substituted for about 350 to 500 grammes of bread. After the potatoes were substituted there was always a definite drop in the curves representing the urine and sugar excretion. In none of his cases dld the sugar entirely disappear. Mossé states that there was also a marked amelioration in the patient's symptoms. The thirst became less, neuralgias disappeared, and the strength

increased. He found that after potatoes had been substituted for bread for several days, and then the patient placed on the original amount of bread the excretion of sugar never reached the limit attained previous to the potato régime. The writer consequently holds that a potato diet has a similar beneficial effect to the "hunger-day" of Naunyn.

Good results have followed the use of the potato régime in not only the mild, but also the severe forms of diabetes. Mossé claims that traumatic wounds and those following surgical operations heal much more rapidly on a potato diet, and cites cases attempting to demonstrate this view.

Mossé advances two hypotheses to explain the beneficial effect of the potato diet. The first is that the potato produces a sugar more easily warehoused than that produced from bread; and second, that it introduces a substance into the organism which favors the glycolytic function of the body. The diminution in the thirst is attributed to the greater amount of water contained in the potatoes. The increased glycolysis is believed by the writer to be due to the much greater quantity of potash introduced into the system as a result of the potato diet.

From the series of charts published it seems quite certain that potatoes are better tolerated by diabetics than wheat bread.

On the Typhoid Psychoses.—FARRAR (*The American Journal of Insanity*, July, 1902, p. 17) reports four cases illustrating various types of psychoses observed in connection with typhoid fever. Esquirol at the end of the eighteenth century was the first to call attention to the fact that not infrequently psychoses develop during or following the course of the acute febrile diseases. Since Esquirol's day considerable attention has been paid to the relation between the infections, particularly typhoid fever, and mental disturbances, but its importance has been underestimated. Farrar, in his contribution, endeavors to emphasize the current teaching concerning the effects of typhoid fever on mental functions as expressed particularly by the Kraepelin school.

Typhoid fever attacking a sane individual may leave him free from psychic symptoms or give rise to all gradations of mental disease. The severity of the symptoms does not necessarily stand in relation to the height of the fever or the intensity of the infection. Persons belonging to families with psycopathic tendencies are more prone to alienation, especially the initial delirium, than those not thus burdened. A second or third attack of typhoid is more likely to present mental troubles than the first.

The *initial delirium* is the rarest form of psychical disturbance in typhoid, but it presents the most rapid course and the worst prognosis, over 50 per cent. of the cases ending fatally. The delirium may precede for several days the onset of fever, or the cases may remain afebrile throughout. These cases often lead to errors in diagnosis, and occasionally result in the commitment of the patients to an insane institution.

The *febrile psychoses*, that is, those occurring during the course of the fever, are the commonest. These present the best outlook, although in 25 per cent. the psychical disturbance persists for varying lengths of time into or after convalescence. The febrile psychoses may be divided into two groups. The first comprise the *true fever delirium*, those standing in closest relation with

rise of the fever and disappearing as the temperature becomes normal. They comprise, according to Kraepelin, 75 per cent. of the cases. The second include the psychoses not associated with the development of fever, and outlasting the latter by months or even years. These make up the remaining 25 per cent.

There are lastly the *asthenic psychoses* or those which develop during the period of convalescence. The conditions of exhaustion, anæmia, and malnutrition especially favor the development of some psychical disturbance. According to Kraepelin there are three principal divisions of this type: (1) Isolated delusions or fallacious sense perceptions; (2) conditions of exaltation; (3) conditions of quiet depression, including states of mental weakness. The prognosis of the asthenic forms is slightly better than in the cases with initial delirium, but much less favorable than in the fever psychoses. Kraepelin found that 71.8 per cent. of the patients recovered, 20.5 per cent. developed chronic insanity, and 7.7 per cent. died. In many of the cases which become chronic, inherited predisposition has been noted.

Pulsation in the Second Left Intercostal Space.—For a number of years there has been a difference of opinion as to the part of the heart that causes the localized pulsation in the second left interspace in mitral stenosis. Two main views have been held. Balfour and Sansom still support the view originally advanced by Bouillaud, that the pulsation is due to the systole of the left auricle. The majority of recent writers on this subject, however, agree with the opinion originally brought forward by Hope, that this pulsation arises from the contact of the conus arteriosus of the right ventricle and the pulmonary artery with the chest wall in the vicinity of the second left interspace. This view is supported by Gibson and Osler.

Gibbes (*Edinburgh Medical Journal*, September, 1902, p. 246) publishes the clinical and pathological records of a case of mitral stenosis that support very strongly the latter view. The patient was a male, aged thirty years. On deep expiration, an impulse was plainly visible in the second left interspace, its nearest point to the mid-sternal line being 2¼ inches from the left border of the sternum. The area of pulsation was 1 inch in length, and on auscultation was found to be *presystolic* in rhythm. It was not visible on inspiration. When the heart was inspected *in situ* at autopsy the left auricle and its appendix were invisible. The right auricle and ventricle were very considerably engorged. The conus arteriosus of the right ventricle was markedly dilated and extended well into the second left intercostal space. These relations are well illustrated by a photogravure of the heart *in situ*, and seem to confirm the view that the pulsation is due to the conus arteriosus of the right ventricle. Clinically, it had been observed that this pulsation was presystolic in time. Gibbes' explanation for this was that he believed that the systole of the right ventricle occurred while the left was in diastole. In other words, that a partial asynchronism occurs. He admits that this doctrine is very heterodox, as the upholders of strict synchronism deny the possibility of one ventricle beginning the systole before the other. In support of his theory he says: "At the same time they accept asynchronism as a cause of the reduplicated second sound, and thereby admit that the systole of one ventricle may end before the other—a distinction without a difference."

The So-called "Spotted Fever" of the Rocky Mountains.—WILSON and CHOWNING (*Journal of the American Medical Association*, July 19, 1902, p. 131) have published the results of their study of eleven cases of so-called spotted fever. This malady is confined to a limited area situated on the eastern foothills of the Bitter Root Mountains, a range along the top of which runs the Idaho-Montana line. So far as known it is confined to circumscribed areas of Montana and Idaho on the western side of the Bitter Root Valley.

This spotted fever prevails in the spring months only, and has been known in Idaho for thirty years. There is a preliminary malaise, and the disease is ushered in by a severe chill. The chills recur at intervals throughout the disease. The eruption appears from the second to the fifth day, appearing first on the wrists, ankles, and back and extending over the whole body in twelve hours. The macules are first rose-colored, not elevated, and vary in diameter from 1 to 5 millimetres. At first they disappear, but later persist on pressure. They become dark blue and purpuric in character. The eruption is subsequently confluent and gives a marbled appearance to the body. Desquamation begins in the third week. The spots do not entirely disappear until weeks or months after convalescence is established. The fever may reach 105°. In the cases which recover it begins to fall by lysis at the end of the second week, and reaches normal about the end of the fourth week. The pulse and respiration are high, out of all proportion to the fever. The spleen is always enlarged and tender. There is usually nausea and vomiting in the second week. Jaundice frequently occurs. The bowels are constipated. The urine contains albumin, coarsely granular and blood casts. Hypostatic pneumonia, arthritis, and gangrene of the skin occasionally occur as complications. There is a leucocytosis of about 12,000. The hæmoglobin is in the neighborhood of 50 per cent. The Widal reaction is negative for typhoid fever. The great majority of the cases belong to a very severe type, of which from 70 to 80 per cent die.

The observers were able to make autopsies on six cases. The only striking gross lesion is the enlarged spleen and petechiæ of some of the serous membranes. There are no intestinal ulcers; no evidences of meningitis.

The investigators were most interested in the etiology of the disease. The cases were studied very carefully bacteriologically, but no organisms of importance were found. The results of the study of the blood were most interesting and important. They found that the red blood cells in practically all the cases contained a hæmatozoon. This in the early stage is ovoidal and resembles somewhat the hyaline body of malaria, but is not amœboid. Sometimes they are in pairs in the red cell. In the second stage they are larger, 2 to 3 microns thick to 3 to 5 microns long. At this stage they are markedly amœboid, protruding and withdrawing pseudopodiæ actively. In a later phase they are again seen in pairs resembling diplococci, and exhibiting active Brownian movement. At no stage is the organism pigmented. These organisms are many times more numerous in the visceral bloodvessels. They stain with the basic aniline dyes. Two rabbits were inoculated with spleen pulp and heart's blood of a fatal case, and these organisms were found in the red cells of the rabbits' blood subsequently. They believe that this organism is very closely related to the Cyrosoma bigeminum, the organism causing Texas fever.

All the eleven cases that they observed had been bitten by ticks, and Wilson and Chowning believe this insect is the means of transmitting the disease. This tick becomes active about the time the first cases of "spotted fever" appear, and remains active about the same time. They are inclined to the view that the gopher is the host of this parasite among the lower animals and that the disease is transmitted from this animal to man by the tick.

SURGERY.

UNDER THE CHARGE OF

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Lung Complications in Appendicitis.—SONNENBURG (*Centralblatt für Chir.*, 1902, No. 26) states that his experience with cases of perityphlitis shows that the greater number of cases in which there are lung complications originate from emboli; Gussenbauer has had a similar experience. In the hospital at Moabit, out of 740 cases 28 had some lung complication, and of these 14 were cases of thrombosis; and in the private clinic out of 260 cases 19 had some lung complication. In the causation of this complication the anæsthetic plays an entirely subordinate part. Practically every case of perityphlitis has a thrombus, whether pus is present or not. If, in the course of the operation, the thrombus is broken up emboli may make their way into the general circulation. It is certain that these originate in the portal system, probably from the region of the vena cava. The pelvic veins are situated close to the veins of the extremities, and in many cases the usual symptoms, such as pain, œdema, etc., are not present. Septic emboli may appear immediately after the operation or as late as the eighth day; as a rule they are accompanied by a more or less great rise in the temperature. The proper and early diagnosis of lung emboli is of the utmost importance so that a proper treatment may be carried out.

The Covering of the Amputation Stump with the Tendo Achilles.—WILMS (*Centralblatt für Chir.*, 1902, No. 24) states that although Bier has reported satisfactory results from his osteoplastic method of covering in the amputation surface, still the all-important question of stump formation and treatment is still open to discussion. The author states that he has had good results in amputations of the log by covering in the end of the tibia with the tendo Achilles. Experience with the method of Bier has shown that it is not always possible to strengthen or render hypertrophic the under sur-

face of the skin by appropriate massage or exercise. In the majority of cases atrophy from pressure is the result. The author performs the amputation in the usual way, except that the tendon is carried over the stump and swerved to the interior surface of the tibia. The one case in which this method was used was a complete success in every way.

The Treatment of Syphilis by the Injection of Yellow Oxide of Mercury.—LOISON (*Archives de Méd. et de Pharm. Militaires*, 1902, No. 1) states that the principal advantages of this method are: 1. The exclusion of all deceit upon the part of the patient in the application of the treatment. 2. It permits of exact dosage. 3. The avoidance of irritation of the intestinal canal. 4. The skin and linen of the patient are not soiled, as happens when inunctions are used. 5. The therapeutic results are rapid and effectual.

Spinal Anæsthesia with Tropa-cocaine.—NEUGEBAUER (*Wiener klin. Woch.*, No. 50–52, 1901, abstracted in *Centralblatt für Chir.*, 1902, No. 31) states that Schwartz has reported very satisfactory results with this drug in doses of 0.25 c.cm.; Bier has had a similar experience. The solution should be freshly prepared each time. The instruments should not be laid in carbolic solution before use, for in two cases in which this was done poisoning resulted. Anæsthesia usually begins at the end of a minute, and appears first in the perineum, then the genitalia, the posterior portion of the thigh, the feet, the legs, and finally in the inguinal and abdominal regions. In the lower extremities one may be sure of absolute anæsthesia of the skin incisions, and almost always of the deeper tissues and bones. The serosa remained painful in a Bassini operation and also in an extirpation of the rectum. The anæsthesia remained longer in many cases in operations on the extremities in the leg which was full of blood than in the other one in which the circulation was normal. In 39 cases a 0.005 c.cm. solution was used with success, and in 18 cases 0.006 c.cm. The stronger solution undoubtedly gives a longer period of anæsthesia. The author states, in conclusion, that a freshly prepared dose of 0.05 or 0.06 c.cm. of tropa-cocaine is an absolutely sure and harmless method of inducing anæsthesia of the lower extremities, perineum, and neighboring regions.

The Surgical Treatment of Diseases of the Lungs.—GERULANOS (*Deutsche Aerzte Zeitung*, 1902, Nos. 9 and 10, abstracted in *Centralblatt für Chir.*, No. 30, 1902) states that the great thing to be avoided in all lung operations is pneumothorax. Either one of two methods may be employed: 1. Wall off with tampons the parts surrounding the field of operation. 2. Bring the area of disease out through the incision, and then suture the surrounding region to the parietal pleura. All other methods of promoting artificial adhesion are time-wasting as well as uncertain. The incision into the lung itself is not dangerous; the danger of bleeding never great, and can always be controlled by tampons, for the blood pressure here influences only about one-third of the arteries. The separation of the tissues must not be done with knife or scissors, for the thermocautery cannot be used to stop bleeding from the larger vessels. The chances for the healing up of cavities are better when they are situated in the under portion than when they are in the

upper. The rigidity of the upper portion of the thorax makes necessary an immobilization of the breast wall so as to avoid the intrapulmonary cavity which otherwise results from centrifugal cicatricial atrophy.

Perforation of the Bladder by a Calculus.—LAUWERS (*Jour. de Chir. et Annales de la Soc. Belge de Chir.*, 1902, No. 5) quotes Legueu, who has aptly stated: "Perforation of the bladder may be the result of the ulceration of the bladder by a calculus." Chapplain has reported 29 cases in which the perforation was almost always in the posterior wall, and usually terminated fatally. Peritonitis usually resulted, but in women one may observe the calculus eliminated, without fatal results, through the vagina, and the result is a vesicovaginal fistula. Lauwers in reviewing the literature has found four cases in which the calculus perforated the anterior wall of the bladder, with a resulting abscess of the space of Retzius and urinary fistula of the anterior abdominal wall. The author's case was a youth, aged nineteen years, of poor physical and mental development. Examination showed a urinary fistula of the abdominal wall, situated in the median line about five or six finger-breadths above the symphysis pubis. The skin opening was the size of a fifty-centime piece. A metal catheter was introduced through the urethra, and on entering the bladder it came against a large calculus, fixed and occupying practically all of that organ. The patient stated that his disease began as an abscess in the hypogastric region which opened spontaneously and which, after prolonged suppuration, became a urinary fistula. Undoubtedly the way in which this fistula originated was by the calculus causing ulceration and eventually perforation of the anterior wall of the bladder, through which the infected urine passed and caused the prevesical abscess which opened spontaneously, and the fistula resulted. Operation being decided upon the calculus was removed by the hypogastric route. The bladder was thoroughly irrigated with a hot solution of boric acid, and then a metal catheter was introduced through the urethra into the bladder between the calculus and the anterior wall of the bladder. This catheter was held exactly in the median line by an assistant. The abdominal wall was rendered as aseptic as possible and the orifice of the fistula closed with a sterile compress. The transverse incision of Kocher was then made at the level of the superior border of the symphysis pubis. This incision was gradually deepened, and examination showed that the infection had destroyed the prevesical space, and the loose connective tissue of the space of Retzius was transformed into a hard pad of fibrous tissue through which passed the fistula. On opening the peritoneal cavity it was found to be walled off to the right by adhesions between the parietal peritoneum and the peritoneal covering of the posterior surface of the bladder. Some omentum was adherent to the top of the bladder —this was tied off and cut. The peritoneal cavity above and to the left was walled off with sterile pads, and then the greatly thickened posterior wall of the bladder was incised in the median line, and a large phosphatic calculus weighing a little more than forty grammes was removed. The wound in the bladder was closed, as also that in the peritoneum, and finally that in the skin, except for a small area through which a drain of iodoform gauze was passed. The patient made an uninterrupted recovery. Chapplain has reported four similar cases with three deaths. The author states, in conclusion, that early

surgical interference should be followed by success in the greater majority of such cases. This should consist in opening and thoroughly draining the inflammation of the space of Retzius just as soon as it appears, and if possible the calculus should be removed. If of small size it should be removed through the fistulous tract, but if the stone is large or the fistula is small, long, or tortuous the calculus should be removed by either the perineal or suprapubic routes, and of the two the perineal route is, as a rule, the method of choice.

The Primary Suture Treatment of Fractures.—Völcker (*Centralblatt für Chir.*, 1902, No. 26) states that it is an assured fact that a good result in a case of fracture depends upon the replacement of the fragments, and the experience of the last few years has shown that under careful asepsis one may cut down on the fractures when there has been a bad result, break up the adhesions, freshen up the ends of the bone, and then place and maintain the fragments in good position by either wires, or screws, or some other appropriate appliance. Experience in the Heidelberg clinic has shown that the indications for the operative treatment of subcutaneous fractures are only limited. In many cases, especially those of separation or fracture of the epiphyses, is the operation a difficult one, and in every case there is the danger of infection. The cases so treated, as a rule, unite much more slowly than when not sutured, and a fistula may result. The principal indication for the use of the primary suture is in those cases of compound fracture where operative interference is a necessity. This operation is indicated in double fractures of the same limb. Experience has shown that those fractures where one is most anxious to get a good result, as in those involving a joint, the primary suture method has not proved to be a success, but future experience may prove that it will have some value in this type of cases.

THERAPEUTICS.

UNDER THE CHARGE OF

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Physiological Action of Male Fern.—Dr. W. Straub has been experimenting on the extract of male fern, the active ingedients of which are now considered to be filicic acid, flavaspidic acid, albaspidin, aspidinol, and derivatives of phloroglucin. By experiments on frogs he found that the lethal dose for filicic and flavaspidic acids was 2 mg., and for aspidinol and albaspidin 1 mg. for every 50 grammes of body weight of decomposition

products. The filicinic acid butylamin proved to be about five times weaker than filicic acid, while filicinic acid itself was innocuous. To study the effects of these various substances it was not considered advisable to note the irritability of the poisoned muscles toward the electric current, but, instead, the "demarcation current" of Du Bois-Raymond was employed, which occurs when one end of the muscle is suspended in a solution of the drug to be tested. Since with proper concentration a maximum current was obtained, the immersion acted like an artificial transverse division of the muscle; in other words, that portion which came in contact with the solutions was dead, and the principles of male fern were direct muscle poisons. The action on nerve tissues was much less pronounced, and it seemed as if the primary irritability of the nerve trunks was not altered. In arranging the different principles and their derivatives in order of their strength it was found that phloroglucin, filicinic, and butyric acids were inactive; of the remainder the filicinic acid butylamin was least active, then followed aspidinol, flavaspidic acid, albaspidin, and finally filicic acid as most potent. For protozoa the order of toxicity was somewhat different; thus, albaspidin, filicic acid, flavaspidic acid. A number of other non-vertebrates were tested, from colenteates to crustaceæ, and in all, with the exception of certain echinodermata, the great virulence of male fern was demonstrated, and its active principles proved to be strong poison for all kinds of organized plasma, but more particularly for muscle tissue. This was most beautifully shown in the case of worms, and the empirical use of male fern as an anthelmintic finds its scientific proof in these experiments. Since the general experience was that pure filicic acid was much less reliable for therapeutic purposes than the extract, attempts were made to follow its destiny in the organism, and it was found that most of it suffered decomposition, most probably in the intestines.—*Archiv für Experimental Pathologie und Pharmacologie*, 1902, Band xlviii., p. 10.

Alcoholism in Children.—Dr. J. Grosz says that acute alcoholism which is seen occasionally in children presents similar symptoms to those seen in adults. He saw two patients who were brought to the hospital unconscious, with tonic and clonic convulsions, who were controlled by enemata of chloral. The diagnosis was made by the odor of the breath. Several hours of deep sleep followed the disappearance of the convulsions, and one of the patients—a child, aged three years—on awaking asked the nurse for some brandy. In children, therefore, acute alcoholism takes a more intense form than in adults, as convulsions are not seen in the latter. Stimulation of the central nervous system follows the use of small doses of alcohol in children; but this is only apparent, for invariably it is followed by paralysis. The temperature of the body is lowered only by large doses of alcohol, which are very injurious to the organs of the body. Many parents, having the false point of view that alcohol strengthens the body, give small doses to children for a long time, and sometimes it is even given during the nursing period. From one-half to one teaspoonful or more of cognac or tokay, concentrated or diluted, are the quantities usually given. The stimulation of the gastric mucosa produces a dyspepsia which may go on and produce a severe gastritis. Beer and light wines may have the same

result. While parents among the higher and middle classes give their children wine, beer, and cognac, those among the poorer classes usually give brandy and whiskey. Cases of alcohol habituation are seen in infancy when, without regard to the presence or absence of fever or to the weakness or strength of the heart, physicians order or sanction the use of alcohol in sickness. Continuous use of alcohol frequently produces cirrhosis of the liver, and four of such cases, in which malaria and lues had been excluded, were observed by the author. The profound effect which the early use of alcohol in large quantities has upon the nervous mechanism is shown by the cases of epilepsy, chorea, and severe neurasthenia traced directly to its use. In children the production of alcoholism is due largely to heredity, several cases having been described, in the literature, of children who, although removed from their alcoholic parents to favorable surroundings, still in the course of time betrayed unmistakable propensities for alcohol. Demme has found that among the offspring of alcoholics the mortality is extraordinary; that those who survive constitute a sad class of idiots, epileptics, and otherwise neurotic individuals, and that only a very small proportion become useful members of society. Alcohol, in spite of the baneful results of its vicious use in childhood, has distinct therapeutic uses, such as in the cardiac asthenia accompanying diphtheria, measles, scarlet fever, and typhoid, in the collapse associated with intestinal diseases, and with severe hemorrhages. Binz has shown that in the failure or in the total cessation of nutrition the administration of alcohol tends to save the destruction of the tissues. When given greatly diluted in water it is rapidly broken up and totally consumed in the tissues, with the production of carbon dioxide and water. Hence alcohol may serve, not as a nutriment, but as a powerful preserver of the tissues in conditions of permanent disturbances of nutrition, in cases of rickets, scrofula, tuberculosis, and in general in all chronic diseases with lowering of the vital resistance.—*Archiv für Kinderheilkunde*, 1902, Heft 1, S. 15.

Mercury in the Cure of Syphilis.—Dr. Leredde says that on account of the widespread extension of syphilis, acquired and hereditary, and of its being regarded as the active or contributory cause of a larger number of other conditions, its treatment is of primary and essential importance. He lays down the following principles: (1) It is necessary to treat severe symptoms of syphilis by injections of mercury alone; (2) it is necessary to increase the dose of mercury so given until symptoms are influenced by it. He argues that the injection of mercury is better than any other means of administration, because by it the quantity given is absolutely known—a fact which is absent alike in administering it by inunction or by the stomach, as no one can tell how much will be absorbed either by the skin or by the digestive apparatus. The therapeutic effect of injection of mercury depends somewhat upon the dose of the drug given and also upon the form. The disease in one person will not, of course, be influenced by the same quantity as would cure another; and, too, in a given patient the dose must be slowly raised until the desired effect is reached. He recommends, as a preventive of the bad results of mercury, that early in the treatment of syphilis every patient should be sent to a competent dentist to have his teeth cleaned

and filled and to be instructed in the care of his mouth, as he believes that all mercurial inflammations of the mouth start from bad teeth and bad oral hygiene. This he states very emphatically, saying that a dose which causes trouble when the mouth is dirty and the teeth decayed will cease to inconvenience when these conditions are removed. At present, mercury by injection is given usually in a single dose of large size, once or twice a week; but Leredde states that, in order to gain complete and rapid control over the serious signs of this dreaded disease, it is better to give a smaller dose every day for a short time, so balanced as to come just within the signs of chronic mercurial poisoning: for example, if the stronger salts be employed (the cyanides or sublimide), doses of ½ or ¾ of a grain should be given; of the weaker salts (benzoate or biniodide), practically twice the above quantities may be employed daily, instead of the larger doses of salts, like calomel, twice a week, of 1 or 1½ grains each. He believes that the profession underestimate the influence of mercury upon syphilis, and that the quantity given in grave cases is too small, and this is the cause of unsatisfactory results.—*La Semaine médicale*, 1902, No. 17, p.137.

Action of Oil of Turpentine in Phosphorus Poisoning.—Dr. V. Plavec found the lethal dose of phosphorus for a dog weighing 6 to 9 kilogrammes to be 0.02 to 0.03 grammes. Dogs which had received larger doses succumbed in approximately the same time (nine to thirty-six hours), though some of them had received the oil. Of animals with just fatal doses, seven were observed without treatment, while to ten the antidote was administered. Of the first series six died, and of the second, seven, and all those that survived showed severe symptoms. In all cases the commercial rectified oil, poor in oxygen, was employed. The autopsy showed transudation into both pleuræ and into the periœsophageal tissues, pulmonary œdema, passive hyperæmia, clouding of the parenchymatous organs, and hemorrhagic injection of the mucous membrane of the duodenum. In older cases, fatty degeneration and hemorrhage were pronounced. Phosphorus could never be detected in the urine, but where oil of turpentine was given the reaction for this was positive. The author comes to the conclusion that the administration of the rectified oil has no antidotal action on absorbed phosphorus, or at least only such a remote chemical action that would render it valueless for therapy. The same facts have been already determined by others for the oxidized oil.—*Archiv für Pathologie und Pharmacologie*, 1902, Band xlviii., p. 150.

Action of Digitalin by Exocardial Application.—Dr. A. Benedicent, stimulated by the difference in results which certain authors obtained by applying helleborin to the exterior of the heart than when it is allowed to affect the interior of that organ by its presence in the circulating fluid, has repeated the experiments with the drugs of the digitalis group. When digitalin was applied to the normal heart of a frog, no change except a slight increase in the pulse-rate is noticed for a time. This soon sinks very markedly, however, and, while the pulse-volume reaches its maximum, increases slowly until complete stoppage occurs for a short period. This is soon followed by a series of pulsations, and then again by stoppage; then

occur, instead of groups, single contractions interrupted by long periods of inactivity, which increase gradually up to cessation of all heart action in diastole. When, instead of digitalin, other members of the digitalis group —such as strophanthin, scillain, convallamarin, and others—were employed, the same phenomena were observed. There was also noticed a tendency of the heart to attain a systolic position when the poisons were applied both to the inner and the outer side of the heart. The pulse-curve given by the combined application of digitalin and atropine is the same as when digitalin alone was used. From further experiments made to ascertain the effect of an increased temperature on the inner and outer surface of the heart it was found that the outer surface is rendered warmer, the pulse-volume first diminishing, and then increasing with an increase in the pulse frequency. The diastoles finally increase, and the systoles become more and more weak and incomplete. If, however, the rise of temperature be permitted to act upon the heart cavity, simply an exaggerated action of the heart occurs. It beats regularly for hours, and only gradually do the systoles become incomplete until the heart stops in a half-systolic position. These experiments all prove a different arrangement of the inner and outer muscular fibres or a different innervation of the two surfaces.—*Archiv für Experimental Pathologie und Pharmakologie*, 1902, Band xlvii., p. 360.

Acute Alum Poisoning.—Dr. Julius Kramolik reports the case of a young man, aged thirty years, who by mistake drank a swallow of an approximately 10 per cent. solution of alum which he had prepared as a gargle for a sore-throat. Neither the mouth nor the throat showed any marked reaction to the irritant, but the patient vomited thirty-nine times within the forty-eight hours following the ingestion of the alum. Palpation of the stomach was painful. Mucus was found in the vomitus, mingled with blood, imparting a chocolate color to the mass. The urine was stained by blood, and showed morphologically numerous red blood cells, few leucocytes, and few hyaline casts. Traces of albumin were also present. The patient was ill for at least thirteen days.—*Pester Medicinisch-chirurgisch Presse*, 1902, No. 11, p. 242.

Treatment of Addison's Disease.—Dr. Edgard Hirtz suggests that the antituberculous treatment of this affection is entitled to consideration. On this theory, superalimentation and attention to the renal secretions are very essential. Milk, eggs, and light wines are advisable. Lecithin, sodium cacodylate, glycerophosphates, and inhalations of oxygen are useful. Reports from various observers would seem to show the value, in some instances, of opotherapy. The author gives the suprarenal capsules of one-sixth of a grain, two to four times a day. Subcutaneous injections as employed by D'Arsonval are also recommended.—*La Médecine Moderne*, 1902, No. 21, p. 169.

Difference Between Illuminating Gas and Carbon Monoxide Poisoning.—Drs. F. Ferchland and E. Vahlen have found fundamental differences in the symptoms of these two gases which do not permit of the generally accepted conclusion that the average composition of illuminating gas having

been found to be hydrogen 45 to 50 per cent., hydrocarbons 35 per cent., carbon monoxide 2 to 3 per cent., of these the hydrocarbons have only a slight narcotic effect, and all the other ingredients, except carbon monoxide, are harmless, so that it would seem safe to ascribe to this latter constituent the toxicity. They found in experimenting with frogs that the illuminating gas proved to be much more poisonous than pure carbon monoxide, despite the fact that the former in this instance contained but 9.7 per cent. of the latter. To what illuminating gas owes its increased toxicity it was impossible to decide, owing to its complex composition.—*Archiv für Pathologie und Pharmakologie*, 1902, Band xlviii., p. 106.

PEDIATRICS.

UNDER THE CHARGE OF

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Two Cases of Congenital Disease of the Left Heart.—THEODORE FISHER (*British Medical Journal*, March 15, 1902, p. 639) reports two cases of congenital disease of the left heart in infants, with the post-mortem findings in each case. The first case was a rather small, anæmic male infant, aged fifteen months. There was a slight degree of cyanosis, but no clubbing of the fingers. The mother stated that at birth the child was very blue, and at frequent intervals since had suffered attacks of dyspnœa, upon which occasions cyanosis was marked. The apex-beat was in the fifth interspace, about one-quarter of an inch outside the nipple line. A high-pitched systolic murmur was heard over the entire cardiac area, but was not transmitted beyond the limits of the heart nor heard behind. The second sound at the pulmonary cartilage was sharp, but elsewhere was rather dull. At the apex three sounds were audible, with something of a *bruit de galop* rhythm. At autopsy the heart was found much hypertrophied, the enlargement being mainly of the right ventricle. The pulmonary artery was double the size of the aorta. The tricuspid orifice was unusually large, while the mitral was stenosed, the latter measuring but 5 mm. across. In addition to the thickened and drawn-together flaps of the valves, as in ordinary mitral stenosis, there was present a perforated diaphragm formed by a circular membrane, and attached to the bases of the mitral flaps. The aorta was constricted above the point of entry of the ductus arteriosus. The ductus arteriosus was patent, while the septum ventriculorum and foramen ovale were normal.

The second case was one of aortic stenosis, in an infant, aged four and a half months, in which the segments of the aortic valves were much thickened

and adherent to one another. The left ventricle was hypertrophied; the other valvular orifices were normal. An interesting fact in connection with this case was that about three months before the birth of the child the mother had suffered from a painful swelling of the knee, which lasted a few days.

The writer has been able to find few records of cases of congenital mitral stenosis. In the first case described the origin of the perforated diaphragm is obscure. It is difficult to see how it could have been produced by endocarditis, since the membrane did not occupy the usual site of rheumatic vegetations. Instances of congenital aortic stenosis are more numerous, Rauchfuss having recorded twenty-four cases, the majority of which were apparently due to endocarditis. Cases in which two segments of an aortic valve are adherent to one another are not rare, but whether such a condition is due to endocarditis or is a malformation is not clear. It is a curious fact that when only two aortic segments are present the valve is more likely to become affected with endocarditis during adult life than when the normal three segments are present. Parkes Weber argues from this that in some of the cases of aortic disease in adults, where two segments are found adherent, the adhesion has really existed from fœtal life. On the other hand, Fisher has met with specimens in the post-mortem room which illustrate various stages in the development of such adhesions during adult life. The disease is one of adult life, yet it is possible that a similar inflammation may attack the valves of the fœtus. This would be especially probable if one could connect the valvular disease with syphilis, but of such an association there seems to be little evidence. While, however, other causes of fœtal endocarditis besides rheumatism may exist, in the case of congenital disease of the aortic valves recorded above, the thickening, although well marked, resembled that commonly seen in rheumatism, and the history given by the mother leaves little doubt that rheumatism was the cause.

Euquinine in Pediatric Practice.—Rocaz, in a communication to the Société de Médecine et de Chirurgie de Bordeaux, February 14, 1902 (*Revue Mensuelle des Maladies de l'Enfance*, July, 1902, p. 330) considers the availability of this drug for administration to children, because of its almost total lack of unpleasant taste. Euquinine is the ethylcarbonic ether of quinine, occurring as white, needle-like crystals, melting at 203° F., sparingly soluble in water, but very readily in ether, chloroform, and alcohol. With acids it forms salts which are equally insoluble in water, except the chlorhydrate, which is very soluble and has a very unpleasant taste, presenting no advantages over the chlorhydrate of quinine. In his investigations Rocaz has always used the euquinine, and not its salts, administering it in suspension in a coffeespoonful of sugar-water. It was always taken without repugnance. In several cases in which it was thus prescribed and readily taken, the administration of quinine by the mouth had been impossible. It also has the advantage of being well tolerated by the digestive tract even when given in massive doses.

Experiments to test the absorption of euquinine showed that elimination by the urine began between the first and second hour after administration, reaching its maximum after seven hours. These conclusions agree with

those of Gamarelli, in Italy, except that this observer found elimination to begin from the ingestion of the drug.

Euquinine is therefore absorbed and produces all the effects of quinine medication. Its indications in pediatric practice are the same as those of the alkaloid from which it is derived. Its contraindications are not so numerous, since it is better borne by the digestive organs.

The dosage is higher than that of quinine—from one and a half to twice as great. Thus, during the first year Rocaz uses from 10 to 15 centigrammes a day (1½ to 2½ grains); from one to two years, 20 to 30 centigrammes (3 to 4½ grains); from two to four years, 30 to 60 centigrammes (4½ to 9 grains); from three to six years, 40 to 80 centigrammes (6 to 12 grains), and from six to ten years, 60 centigrammes to 1 gramme (9 to 15 grains).

GYNECOLOGY.

UNDER THE CHARGE OF

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The Mesometrium.—THEILHABER and MEIER (*Archiv für Gynäkologie*, Band lxvi., Heft 1) think that too little attention has been paid to the pathology of the mesometrium (muscular wall of the uterus). Many cases of menorrhagia and leucorrhœa are due not to inflammatory changes—the so-called chronic metritis—but to muscular insufficiency, leading to blood stasis and hypertrophy of the mucous and muscular layers, with their resulting symptoms.

They distinguish several clinical types, viz.: "Hypoplasia" in anæmic girls; "myo-degeneration" following infection; "myofibrosis," or the physiological change occurring at the menopause; changes in the uterus accompanying disease of the adnexa, and myomatous conditions.

Sixty-one uteri were examined by the authors with special reference to the relation of the muscles to the connective tissue and vessels. In the majority of the cases in which menorrhagia and leucorrhœa had been marked there was an excess of connective tissue. Atheroma of the vessels was present in the hemorrhagic cases as well as atrophy of the uterine muscles. The changes in the vessel walls indicated physiological arteritis obliterans rather than true arterio-sclerosis.

Prophylaxis of Gonorrhœa.—GREIFE (*Centralblatt für Gynäkologie*, 1902, No. 28) divides all cases into two classes—prostitutes, and married women who are infected through their husbands. He urges the necessity of more careful training of young men in regard to sexual morality, as well as the

systematic inspection of all public women, whether healthy or unhealthy, including routine microscopic examinations of vaginal discharges. The use of prophylactic urethral injections of a 20 per cent. solution of protargol after coitus is recommended.

Men who contemplate matrimony should be taught that they may infect their wives long after all visible evidences of the disease have disappeared; hence the physician should not pronounce the patient cured until repeated examinations have failed to show the presence of gonococci. The bride's parents should refuse to allow her to marry without positive evidence from the young man's doctor (!). A man who marries after having once had gonorrhœa should observe the following rules: To pass his urine immediately before intercourse; never to perform the act while intoxicated; to avoid repeated coitus, and if it takes place again within twenty-four hours the woman should take an antiseptic douche afterward. Such injections should also be frequently repeated.

[While we agree heartily with most of the writer's conclusions, it would seem as if marriage should be absolutely forbidden as long as these precautions against possible infection must still be observed.—Ed.]

Acute Oophoritis.—Skrobansky (*Journ. Akusch. i shensk. bolesnig; Centralblatt für Gynäkologie*, 1902, No. 30) examined twenty-five ovaries removed from females between one and twenty-seven years of age who had died from infectious diseases. The majority of cases were those of scarlatina and diphtheria. The writer concludes that the ripe as well as primordial follicles are destroyed. The membrana granulosa of the younger follicles, however, sometimes persists for a long time, the flat cells being changed to cylindrical. In follicles in which the ova undergo granular degeneration of the protoplasma and chromatolysis of the nucleus these cells may assume a phagocytic power. The destruction of the ripe follicles resembles the physiological atrophy. The histological changes are the same, without regard to the nature, severity, or duration of the infection.

Colpotomy in Pyosalpinx.—Treub (*Revue de Gynécologie*, 1902, No. 6) reports seventy-nine cases of vaginal incision and drainage, sixty-six being cases of pyosalpinx and thirteen of hydrosalpinx. Two patients died of pyæmia (puerperal). Many were only temporarily benefited; forty-four patients were cured, often only after several months had elapsed.

The writer does not believe that hydrosalpinx can be cured by simple incision any more than hydrocele. Tuberculosis is, of course, not affected. He concludes that total vaginal extirpation is the only treatment for pyosalpinx and tuberculosis of the tubes.

Treatment of Pruritus.—Siebourg (*Centralblatt für Gynäkologie*, 1901, No. 26) recommends hypodermic injections of saline solution over the affected area, with the view of causing cutaneous anæsthesia, as much as 10 ounces being used at a time. He speaks highly of an ointment containing 30 grains of muriate of cocaine, 20 grains of orthoform, 8 grains of menthol, and 15 grains of carbolic acid to 5 drachms of vaseline.

In chronic cases in which the skin and mucous membrane are unbroken he applies a solution containing 1 per cent. of salicylic acid and 2 per cent.

of resorcin. He also injects hypodermically weak solutions of cocaine and carbolic acid.

LEREDDE (*Société de Thérapeutique; La Gynecologie*, 1901, No. 6) speaks highly of the interrupted current in long-standing cases of pruritus which have resisted all methods of treatment. Two or three séances weekly, lasting fifteen minutes, effected a cure in every case treated by him within from two to four weeks. The writer emphasizes the importance of frequent interruptions.

Tuberculosis of the Vagina.—SPRINGER (*Zeitschrift für Heilkunde*, Band iii., Heft 1) states that only twelve cases of vaginal tuberculosis had been recorded by Chiari in the course of ten years, representing 15 per cent. of all cases of genital tuberculosis. This fact would seem to show that the vagina offers a powerful barrier to the invasion of the bacilli, due to the resistant epithelium, the absence of glands, the reaction of the secretions, or the natural drainage of the canal.

The writer suggests the following ways in which tuberculous infection of the vagina may occur: 1. Direct infection from a tuberculous uterus or urinary tract, from the tuberculous bowel, Douglas' pouch, peritoneum, or vulva. 2. Infection through the blood. 3. By direct contact, coitus, infected fingers, pessaries, etc.

Peritonization in Laparotomy.—Under this term JUDET (*La Gynécologie*, April 15, 1902) refers to the covering of all raw surfaces within the pelvis with flaps of healthy peritoneum, in order to prevent septic infection and intestinal adhesions. He discusses at considerable length the advantage of this method as compared with gauze tamponade, and the technique of different operators, but lays more stress upon immediate than remote results.

[While operators will agree with the writer in his recommendation to cover all raw surfaces with peritoneum wherever this is possible, it must be confessed that he touches but lightly on the difficulty of accomplishing this in cases in which there are extensive intrapelvic adhesions.—H. C. C.]

Ileus Cured with Atropine.—MÜNCHMEYER (*Centralblatt für Gynäkologie*, 1902, No. 16) reports a case of intestinal obstruction occurring on the third day after myomectomy, the symptoms by the fifth day becoming so serious that it was proposed to establish an artificial anus. Previous to adopting this procedure, atropine, gr. $\frac{1}{3}$ (0.002 gm.), was administered hypodermically, although the patient was fifty-two years of age. Six hours later flatus passed, and twenty hours after the administration of the drug the patient had several normal dejections and made a rapid convalescence. The author recommends that this treatment be adopted in all similar cases before resorting to a secondary operation.

In the discussion following the report of this case Osterloh did not favor the atropine treatment, preferring lavage of the stomach. The reporter replied that the serious nature of the case and the rapid relief of the obstruction fully justified it.

[Remembering the intolerance of some patients to this powerful alkaloid, it would seem wiser to give small and repeated doses, and not to wait until the case has progressed so far that heroic treatment becomes necessary.—H. C. C.]

OBSTETRICS.

UNDER THE CHARGE OF

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Removal of Uterine Myoma Through the Vagina without Interrupting Pregnancy.—In the *Centralblatt für Gynäkologie*, 1902, No. 21, SEELIGMAN reports a case illustrating the extraordinary tolerance displayed by the pregnant uterus to manipulation.

The patient was a multipara, aged thirty-four years, who was pregnant about four weeks. She was seized with violent uterine hemorrhage, and examination revealed a large, firm, submucous myoma in the lower portion of the womb. The hemorrhage was so excessive that a firm tampon was applied, transfusion with salt solution practised, and five days were allowed to pass before an effort could be made to remove the tumor. The tumor was removed in pieces, and to check the hemorrhage the uterine cavity was firmly tamponed with iodoform gauze. The patient made a good recovery, and was discharged from the hospital in three weeks. Her pregnancy remained uninterrupted, and she was delivered spontaneously of a living child at term.

The most rational explanation for this remarkable case is that the ovum had embedded in the upper and anterior wall of the uterus, while the tumor was upon the posterior and inferior portion. In spite of this, it is remarkable that the pregnancy was not interrupted.

The Treatment of Postpartum Hemorrhage.—HENKEL, in the treatment of postpartum hemorrhage (*Centralblatt für Gynäkologie*, 1902, No. 21), has found it of value to tampon the lower uterine segment and cervix only, carrying the cervix strongly backward and bringing the fundus forward against the pubes. He has found this better than tamponing the entire cavity of the uterus, because this method brings about anteflexion and places the tampon upon the most relaxed portion of the womb.

He has also found it of value, in cases in which hemorrhage was threatened, to give ergot during the latter portion of labor in tonic doses. In cases of retained placenta where hemorrhage begins and the placenta must be removed he finds it of advantage to employ chloroform anæsthesia during the expression of the placenta. In lacerations of the cervix where bleeding occurs from the cervical arteries he has applied tenaculum forceps to the two lips of the cervix, allowing them to remain from twelve to twenty hours. In addition, he uses a tampon of iodoform gauze, and has seen none but good results from this practice.

[We fail to observe the advantage in the use of tenaculum forceps to check hemorrhage from the cervix over the application of one or more

stitches of chromicized catgut. The use of stitches has an additional advantage that certainly in some cases union of a torn cervix is thereby promoted. The passing of stitches is attended with little difficulty, and to our minds is far more satisfactory than the application of forceps.]

Albuminuria in Pregnancy.—At a meeting of the Obstetrical Society of Berlin, VEIT (*Centralblatt für Gynäkologie*, 1902, No. 21), in a paper upon this subject, calls attention to the influence exerted in the production of albuminuria by syncytial cells and by other embryonal tissues carried to different parts of the mother's body in emboli and thrombi. This question suggested the possibility of producing artificial immunity to this malignant action of the embryo by the injection of placental tissue.

Veit's paper calls attention to some modern researches upon the rôle played by the placenta which lead us to believe that the after-birth is not a medium for the passage of oxygen only, but that it is analogous to the thymus or thyroid in its influence upon the metabolism of the mother.

In the discussion of this paper, Gottschalk drew attention to his paper in the *Archiv für Gynäkologie*, Band xlvi. p. 56, in which he ascribed the changes found in the kidneys of the pregnant patient to emboli of syncytial cells. Diseases of the placenta or accident to the placenta would lead to the involvement of the kidneys which might result in eclampsia.

Albuminuria during Labor.—In the *Archiv für Gynäkologie*, 1902, Band lxvi., Heft 2, ZANGEMEISTER contributes an extensive paper upon this subject based upon observations made at the Leipsic clinic.

In estimating the frequency of albuminuria occurring in patients actually in labor widely differing results are reported. Thus Meyer reports 41 per cent. of patients in labor having albumin in the urine; Litzman, 44 per cent.; Winckel, 20 per cent.; Petit, 15 per cent.; Möricke, 37 per cent.; Ingersley, 33 per cent.; Lantos, 59 per cent.; Fleischlen, 17 per cent.; Meyer in 1138 cases, 25 per cent.; Aufrecht, 56 per cent.; Trantenroth, 99 per cent.; Friedeberg, 45 per cent.; Pajikull, 100 per cent.; and Saft, 28 per cent.

So far as the quantity of urine voided is concerned, the greatest quantity is seen in the morning, the least at night. So far as the period of pregnancy is concerned, the diuresis increases in the thirty-ninth week, and is less from thence on until labor.

In estimating the occurrence of albuminuria during pregnancy the results of various observers differ from 1 to 50 per cent., the average showing that from 4 to 0.7 per cent. have albumin during pregnancy. After describing the methods employed in the study of these cases, Zangemeister states his conclusions, which are essentially as follows: During pregnancy in healthy women a progressively increasing diuresis occurs, which is notably greater as labor approaches. When parturition begins the diuresis diminishes, and the quantity of urine voided is about one-third of that previously voided during the last months of pregnancy. Immediately after labor there is another increase in the quantity of urine excreted, which gradually gives place to the normal quantity. Zangemeister found in the last months of pregnancy albumin in the urine of 10 per cent. of cases examined. If repeated examinations were made, albumin was found persistenly during the

last three months of pregnancy in 40 per cent. of cases examined. About 20 per cent. of pregnant women have urine containing casts.

The belief that primiparæ have casts more frequently in the urine than multiparæ with albumin is not accepted by the writer, who found very little difference between primiparæ and multiparæ. During the last two weeks of pregnancy albumin and casts are much more frequent in all classes of pregnant patients. Small quantities of albumin cannot be considered as abnormal during the last months of pregnancy. The persistent presence of casts indicates an essential lesion of the kidney. The influence of labor upon the constitution of the urine is shown in the presence of epithelia in a condition of cloudy swelling, which comes from the kidneys. These are more frequent, and seem more altered as labor proceeds. White and red blood corpuscles are often found in the urine secreted during labor. In small quantities casts are found during labor in the urine of 40 per cent. of cases, both primiparæ and multiparæ. In considerable quantities casts occur in 23 per cent. of primiparæ and in but 12 per cent. of multiparæ. Until the excessive quantity is present, albumin and casts occur in parallel quantities during labor, and the presence of casts at this time cannot be considered pathological. They must be referred to some lesion of the kidneys in existence before labor.

The albuminuria of pregnancy and the albuminuria of labor are by no means identical. Patients showing albuminuria in pregnancy more frequently have albumin during labor. The most reasonable explanation for the albuminuria of pregnancy lies in some failure in the perfect metabolism of the organism and excretion through the kidney.

The albuminuria occurring during labor must be referred to increased blood pressure in the kidneys, caused by uterine contractions and by the disturbance of the circulation seen during labor.

Pneumococcus Meningitis Simulating Puerperal Eclampsia.—WILSON (*Transactions of the Obstetrical Society of London*, 1902, Part I. p. 5) reports the case of a patient admitted to the Birmingham Hospital in a comatose condition. Her pulse was 140, respiration 38, and temperature 100.8° F. She died without recovering consciousness. Examination showed that she was a multipara, between six and seven months pregnant. There was no œdema of the lungs, and the heart was normal. The urine obtained by catheter was of acid reaction; specific gravity, 1032; contained a large quantity of albumin and 1.5 per cent. of sugar. There were no casts or blood corpuscles.

The history was that the patient had borne seven children, and that five days before admission she complained of severe headache and malaise. The day before admission she was found unconscious in her bedroom; passed through a succession of fits, in which the face was drawn to the right side, and feces and urine voided during the attack. The convulsions continued incessantly until the patient was put under the influence of chloroform. The urine was highly albuminous, and the physician called to see the case diagnosed puerperal eclampsia.

On post-mortem examination it was found that death was due to a purulent meningitis caused by the pneumococcus.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

UNDER THE CHARGE OF

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Tuberculous Granuloma of the Nose.—In a paper entitled "Tuberculous and Syphilitic Granulomata of the Nose," by DR. WILLIAM LINCOLN, of Cleveland, Ohio (*Laryngoscope*, January, 1902), two cases are reported, occurring in the cartilaginous nasal septum of two women, aged, respectively, forty and forty-five years.

In the first case a piece of tumor removed for microscopic examination revealed typical tuberculous granulation tissue, with the presence of giant cells; nevertheless, syphilitic clinical history, the presence of ulcers on the hard palate, and the scarred sites of many others led to the treatment by potassium iodide in increasing doses, under which recovery took place, with complete disappearance of the growth, leaving a slight depression at its site.

In the second case the piece of tumor submitted for microscopic inspection showed the ordinary structure of tuberculous granuloma, with giant cells, but without evidence of bacilli. Administration of potassium iodide for a month, alone and combined with mercury, not having produced any diminution in the growth, the whole mass was removed with a sharp curette. Eight months later the patient returned with an exactly similar granuloma occupying an exactly similar site on the opposite side of the cartilage; and at this time she gave unmistakable evidence, physically and bacteriologically, of tuberculosis of the lungs, from which she died four months later. Removal of the tumor had left an ulcer rebellious to treatment. It is presumed by Dr. Lincoln that the first granuloma in this case was an instance of primary tubercle of the nose. A summary of the literature on this subject is incorporated in the paper.

Cyst of the Inferior Turbinal.—DR. RICHMOND MCKINNEY, of Memphis, Tenn., reports this case (*Journal of the American Medical Association*, March 22, 1902). It occurred in a stout colored woman, between thirty and thirty-five years of age, and completely occluded the passage. The growth was incised, giving exit to a thin, seropurulent discharge, about a teaspoonful in bulk. The cavity of the cyst was then freely curetted and cauterized. Recovery was uninterrupted.

Cystic Fibroma of the Nasal Cavity.—DR. MCKINNEY also reports a case of cystic fibroma in a boy, aged twelve years. It presented as a reddish, polypoid tumor, about the size of a hazelnut, pedunculated and apparently springing from about the junction of the cribriform plate of the ethmoid with the anterior cartilaginous septum. It was removed by divulsion, discharging dark, grumous, foul-smelling material, while hemorrhage was very free. The site of implantation, which proved to be the cribriform plate, was

cauterized with the electric cautery. Histological investigation of the growth showed it to be a fibroma.

The X-ray in Determining the Limits of the Frontal Sinus.—Dr. John Howard Philip, of San Francisco, recommends (*Journal of the American Medical Association*, March 22, 1902) this method of determining the character of the diseased sinus before operation, and illustrates his remarks with a reproduction from a radiograph taken for that purpose at the San Francisco Polyclinic.

In view of the fact that there are no frontal sinuses in a great many individuals—in some series of autopsies as many as 14 per cent.—this preliminary investigation would, as suggested by Dr. Philip, prevent injury to cranial contents in such cases about to be operated upon for supposed disease of the sinus.

Morbid Growths of the Maxillary Sinuses.—At the late meeting of the American Laryngological, Rhinological, and Otological Society (*American Medicine*, March 15, 1902) Dr. Robert C. Myles reported four cases of polypi attached to the upper wall of the maxillary sinus and protruding into the nose and rhinopharynx. In each instance relief was obtained by curetting the sinus, and, so far as has been ascertained, there has been no recurrence.

Foreign Bodies in the Accessory Nasal Sinuses.—Löhnberg (*Münchener medicinische Wochenschrift; American Medicine*, March 15, 1902) reports two cases: 1. A man, aged forty years, had his eye destroyed twenty years previously by a bursting gun, the iron splinter lodging finally in the right ethmoid sinus and giving rise to chronic inflammation and nasal polyps. The growth and iron splinter were easily removed by operation.

2. A man, aged thirty-two years, had a piece of a felt hat-band driven through the outer table of the skull into the right frontal sinus during a street brawl. Subacute traumatic empyema of the cavity ensued, which disappeared after operative removal of the piece of felt and drainage into the nasal cavity.

Malignant Disease of the Nose and Accessory Sinuses.—In an extensive paper upon this subject, including tabulations of 188 cases from published records, Prof. Joseph S. Gibb, of Philadelphia (*New York State Journal of Medicine*, January and February, 1902), describes and depicts two cases of his own—one of sarcoma of the nares and the other carcinoma of the nose.

Empyema of the Sphenoidal Sinus.—Dr. Jonathan Wright, of Brooklyn, reports (*Annals of Otology, Rhinology, and Laryngology*, February, 1902) a case of isolated, unilateral, latent empyema of the sphenoidal sinus, with delirium and mental symptoms. Operation; recovery. The patient was a physician, fifty-seven years of age, who had an attack of influenza in January, 1901, accompanied with severe coryza and intense pain at the vertex of his head, progressing toward the occiput and down to below the left eye.

After recovery from the influenza this same sort of pain recurred at intervals, becoming more and more severe and almost unbearable. On November 30, 1901, he was first examined by Dr. Wright, who, without detecting anything significant on exploration, came to the conclusion that there was some intracranial difficulty, due most likely to pus under pressure in the left sphenoidal sinus, and perhaps in the posterior ethmoidal cells. Under ether the sphenoidal sinus was opened through the anterior nares and gave exit to dark, cheesy, foul-smelling secretions, and then the middle turbinate was amputated to facilitate drainage. For details the reader is referred to the original.

Spasm of the Larynx.—Under the title of "Vertigo and Ictus of the Larynx" DR. MONCORGÉ, of Mont-Dore, reports (*Annales des Maladies de l'Oreille, du Larynx*, etc., May, 1902) 10 additional cases, which brings up his personal record to 32 out of 120 published cases.

[This variety of laryngismus is usually allied with asthma, whatever the exciting cause of the asthma. When it merely proceeds to giddiness without loss of consciousness it is called by the profession vertigo; when loss of consciousness follows the vertigo, then they call it ictus.]

Myxoma of the Larynx.—PROF. JOSEPH S. GIBB, of Philadelphia, reports (*Annals of Otology, Rhinology, and Laryngology*, February, 1901) a case of myxoma of the larynx occurring in a healthy man fifty-five years of age, who applied for relief of hoarseness of some months' duration. Several masses of a clear homogeneous structure loosely attached by a pedicle were seen beneath the vocal bands, or perhaps attached to the under surface of the left one, which, during phonation, were forced up between and over the vocal bands, preventing proper approximation. The growths were removed in a number of sittings, and were found, upon microscopic examination, to be myxomatous, or, as described by the pathologist, œdematous fibromas or polyps.

OPHTHALMOLOGY.

UNDER THE CHARGE OF

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The Pathogenetic Eventuations of Chalazial Tumors —DR. M. P. WEYMAN (*Annals of Ophthalmology*, October, 1901), makes the following deductions:

Chalazia, from the nature of their structure and pathology, tend to degenerate. This degeneration may be suppurative, more or less acute, and

result in either obliterative inflammation, perforation, and spontaneous cure, or non-obliterative inflammation, perforation, and re-formation. Perforation of this type is usually external.

Chalazia more often break down by a very slow softening and erosive disintegration. During this disintegration the morbid secretions establish fistulous tracts for the purpose of drainage. Chalazia may change in size owing to the intermittency of drainage and the consequent damming up of the irritant discharges and the reactive inflammatory tumefaction. The fistulous drains are of two kinds—natural (by gland ducts) and artificial (by perforation). They show the same pathological conditions as sinuses and fistulæ elsewhere, viz., reactive softening of the inner lining and induration of the circumfistulous tissue, according to the degree and duration of the biochemical irritation of the morbid secretions, lip eversion, and unhealthy granulations of their orifices.

A nipple-like orifice of a Meibomian gland denotes a fistulous duct carrying discharges from a chalazion degenerating within the cartilage; this is mostly observed in the upper lid.

Granulation masses around a conjunctival perforation are not everted chalazial tissue, but unhealthy granulations springing from the bordering edges of the conjunctiva from the constant bathing in irritating discharges.

A hordeolum internum—internal or hardened stye—is a nodular induration around a chalazial sinus. They are most frequent on the lower lid, because gravity, opposing evacuation, keeps the lumen constantly filled, whence the extensive induration. Ordinarily an internal stye shows its true nature by a grayish vesicle upon its body, or a yellowish translucency from within, which often causes them to be incised for regular stye abscesses.

The stagnating morbid secretions in fistulous ducts may soften the septal partitions, and irruptions into healthy glands may take place until the whole cartilage is furrowed and honeycombed. The writer terms this general infection tarsadenitis Meibomica.

Subcutaneous lid abscesses should be attributed to tarsadenitis when the latter exists.

Smooth, dark colored polyps not springing from the internal canthal region are very apt to be the result of old chalazial drains.

Some Functional Disorders of Vision.—EALES (*Birmingham Medical Review*, January, 1902), under the above title, reviews scintillating scotoma, homonymous hemianopsia, temporary monocular blindness, neurasthenic asthenopia, traumatic amblyopia, and hysterical amblyopia.

In scintillating scotoma the attack commences by a sparkling spot or scintillation which suddenly appears near the fixation spot of each eye, persisting upon closure of the eyes. This spot rapidly enlarges, the scintillations being encircled by a bright zigzag line like those of fortifications, while the vision is almost lost. The attack is often accompanied by a feeling of giddiness. This condition persists from a few minutes to half an hour, when it rapidly passes off. Upon recovery of vision headache sets in, which becomes very severe, even prostrating. The visual attack is only the early symptom of an attack of migraine, which commonly but not invariably follows. This affection is very common. Such patients, on account of the pronounced

eye symptoms, seek the advice of the oculist in the hope that their trouble is due to some ocular disorder—a vain hope, usually destined to disappointment.

Homonymous hemianopsia: It is interesting and important to note that a large percentage of these cases of scintillating scotoma pass rapidly into a condition of homonymous hemianopsia. These attacks of hemianopsia last for ten minutes or a quarter of an hour (rarely as long as three-quarters of an hour), and then pass off, usually followed by headache. In the early stage of a fainting fit, before loss of consciousness, hemianopsia is also complained of.

Homonymous hemianopsia can only be produced by some cause affecting the central nervous system posterior to the chiasm, of which it is absolutely pathognomonic. A similar cause would also account for the simultaneous occurrence of identical scintillations near the fixing point of each eye. As these phenomena are so often associated, it seems reasonable to assume that both are due to the same central cause.

The evanescent and recurrent nature of these attacks point to the circulatory disturbance as the cause, while the loss of function and the occurrence of these attacks during fainting point to anæmia of the nerve centres as the actual condition that sets it up, the anæmia being due to vasomotor spasm *per se* in the case of migraine, while in fainting the spasm is due to the tendency of arteries to contract if the intravascular tension is lowered.

The treatment should be the general treatment of migraine, which is often unsatisfactory. By giving saline aperients an attack may be warded off or mitigated. If excitement or fatigue seem to predispose to an attack they should be avoided. If any optical defect is present it should be corrected by means of glasses. In many cases such correction reduces the frequency of attacks. Care should be taken to maintain the general health of these patients.

Temporary monocular blindness: These attacks usually last only a few moments, or from ten minutes to half an hour at most. On examination the eye will be found to be quite normal in all respects. These failures of vision are of daily occurrence, or even several in one day. Such patients are usually anæmic young women.

The fact that many patients suffer frequent attacks for years without any permanent damage to vision justifies the term functional, though a physical basis may be suspected.

The loss of vision appears to be due to a failure of retinal circulation from vasomotor spasm of the retinal artery. Such contraction has been actually observed during an attack. (Benson, *Transactions of the International Ophthalmological Congress.*) In some the failure of vision would seem to be preceded by faintness, which by lowering the general vascular tension facilitates the failure of retinal circulation from vasomotor contraction.

Occasionally an attack, unlike many previous ones, is not followed by recovery of vision. Examination shows all the signs of a block in the artery, with cessation of retinal circulation and œdema of the retina. Such sudden block of the artery until recently was attributed to embolism, but now there is a consensus of opinion that it is due to thrombosis rather than

embolism. These cases where there is a history of previous attacks of temporary loss of vision are taken as strong evidence in favor of thrombosis.

It would seem that blindness ensues when, from a lowered arterial force, the circulation in the retinal artery, whose lumen is diminished by endarteritis, falls below the point required to maintain the visual function. The fact that when a block in the vessel occurs it is usually found at the point where it enters the eye, suggests that the anatomical and physiological condition at this point predisposes it to arteritis and thrombosis.

The prognosis is favorable in the young, where arterial spasm is the usual cause, but in middle life permanent loss of vision, due to thrombosis, may be feared. Iron, nitroglycerin, and strychnine seem indicated in young patients. In middle life a history of syphilis or gout will suggest the line of treatment.

Neurasthenic asthenopia: The patient complains that the eyes are tender to the touch and tire easily; also of pain in the eyes, blurred near vision, lacrymation, and intolerance of light. These symptoms persist after the most perfect correction of any optical error by glasses. The vision will be found normal at first, but can only be maintained a few minutes. The symptoms of general neurasthenia are usually present. The form field is contracted concentrically, and not unequally, as in atrophy of the optic nerve or structural disease of the eye. If the taking of the field is prolonged it becomes smaller, and a fatigue field is obtained. The fields are pathognomonic of this condition.

The most important treatment is the promotion of the general health of the patient.

Traumatic amblyopia is identical with neurasthenic asthenopia, only there has been a history of injury to start the nervous symptoms, which may be as pronounced as those seen in hysteria; so that neurasthenic asthenopia, traumatic amblyopia, and hysterical amblyopia may be considered as degrees of the same affection.

In hysterical amblyopia the color fields may retain their normal relation, but usually the field for red is as large as that for blue or even white. Such a field is pathognomonic of this affection. Frequently there is great difference in the size of the two fields. There often occur in these cases spasms of the various muscles, producing diplopia; spasm of the accommodation, causing myopia. Hemianæsthesia or other symptoms of hysteria are generally present. Hemianæsthesia being on the same side as the supposed blind eye, it is noteworthy that these patients never have an hemianopic field of vision.

The visual defect is regarded as due to a central nervous disturbance. In order to explain the fact that it never conforms to the type of hemianopsia so generally found in structural disease of the cerebrum, it is assumed that there is a second decussation of the fibres of the optic tract, probably about the neighborhood of the corpora quadrigemina, by which the two halves of the fields of vision are reunited, these ending in a higher psychical visual centre, located in the region of the angular gyrus, which thus becomes a visual centre for the eye on the opposite side, and also to some extent for the same side; and that the suppression of the function of this centre leads to the loss of vision in the opposite eye, together with the contraction of the field of vision of the eye on the same side.

DERMATOLOGY.

UNDER THE CHARGE OF

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Parapsoriasis.—BROCQ (*Annales de Dermatologie et de Syphiligraphie*, 1902, No. 4) proposes to call by the above title a series of rare eruptions which have been described by various authors under the names *parakeratosis variegata, exanthème special psoriasiforme et lichénoïde, dermatite psoriasiforme nodulaire, pityriasis lichénoïde chronique, erythrodermies pityriasiques en plaques disséminées*, and *lichen variegatus*. He divides the cases into three principal varieties, viz., guttate parapsoriasis, lichenoid parapsoriasis, and parapsoriasis in plaques. Histologically these cases are characterized by an infiltration of round cells around the papillary vessels which are dilated, by flattening of the papillæ, by marked œdema of the upper part of the derma and the epidermis, by an almost complete disappearance of the germinating layer, by dilatation of the intercellular spaces of the prickle-cell layer and the presence of leucocytes in these spaces, and by œdema of the granular layer which is absent in many places, at which points nuclei are found in the cells of the corneous layer. The duration of these affections is very long. They are not accompanied by itching, nor do they affect the general health. The most effective local application is pyrogallol employed perseveringly and energetically.

Acne and Sycosis Treated by Exposures to Roentgen Rays.—PUSEY (*Journal of Cutaneous and Genito-Urinary Diseases*, May, 1902) reports eleven cases of acne vulgaris and one of sycosis vulgaris treated by exposure to the X-rays. In no case of acne in which such treatment has been carried out for a reasonable period have beneficial results failed to appear, and the author considers this form of treatment an advance over all other methods hitherto employed. All the cases were exposed to a very weak light, using a current just strong enough to illuminate a fairly soft tube. The cases were unusually susceptible, and upon the first sign of erythema or pigmentation the treatment was suspended. The author warns those wishing to use this method of treatment against employing any but the weakest light. In a case of sycosis treated in this manner all evidence of disease had disappeared at the end of three months, and no new lesions have appeared since.

Radiotherapy and Phototherapy.—FREUND (*British Journal of Dermatology*, September, 1902, p. 339) states that all radiant phenomena have the same physical basis. The physical properties of rays as applied to the skin

possess chemical, fluorescent, and electrical properties, the effect varying with the dosage, from mere stimulation to destruction of tissues. In weak dosages the rays favor organic processes, such as growth of hair and production of pigment, but in stronger dosage they lower vitality, produce inflammation or actual necrosis.

Radiant heat, light, electricity, and X-rays similarly influence cell-life. As to the clinical effects of radiotherapy, the physiological effects are in direct proportion to the intensity of the "raying," but are in inverse proportion to the wave lengths. The reactions appear after a latent interval, the length of which is also inversely proportional to the wave-lengths and intensity of the "raying." Those rays which have the property of exciting fluorescence are also physiologically the most powerful. The action of the rays is long persisting. Freund believes that in so-called "D'Arsonvalisation" the effects are solely due to the spark-discharges accompanying the use of the apparatus. All spark-discharges may cause physiological effects, which may result from (*a*) the mechanical bombardment of the tissues, (*b*) the production of heat, (*c*) chemical effects—formation of ozone, and (*d*) ultra-violet ray formation. The effects of sparking vary according to its intensity, being either stimulating or destructive. On the skin they affect the vasomotor system and tend to cause necrosis of the epidermis.

The action of D'Arsonval's apparatus is superficial and due only to the accompanying spark-discharge, and is useful in pruritus, lupus erythematosus acne vulgaris, and pigmentary abnormalities. A simple spark-apparatus consists of a test-tube filled with water and connected with the negative pole of a coil, the positive pole being earthed. With this apparatus Brush-discharges can be obtained equal to those of Oudin's apparatus. The Brush-discharge is useful for widespread areas of disease and in the case of nervous people, the spark-discharge being applicable to more circumscribed areas. Treatment with the "electrified hand" is another spark-method, but a very mild one.

The effective factors in the X-ray method are probably the X-rays themselves and the electric surface tension of the tubes. Vasomotor effects are produced as in ordinary spark discharges. The skin diseases suitable for X-ray treatment are ringworm of the scalp, tinea favosa, sycosis, and hypertrichosis - all diseases in which the chief therapeutic feature is the removal of hair. In this class the X-rays are much more effective than the light rays, but both methods stand much on an equal footing in the remaining class of cases. The depilatory properties of the X-ray tube are due to direct destructive action or to alteration in the blood supply of the follicles. X-rays possess no bactericidal properties.

In comparing the X-ray method and Finsen's light method for lupus vulgaris, Freund states that about the same length of time is required in the two methods, and that the results of both are equally good as regards the scarring. Practically identical results can be obtained with either hard or soft tubes by adapting the time of exposure, strength of current, and distance of the tube. With hard tubes the radiation can be pushed until visible effects are produced, whereas with soft tubes one must work more in the dark and make allowance for reactions before they are visibly manifest. The author regards Finsen's apparatus as superior to Bang's lamp.

PATHOLOGY AND BACTERIOLOGY.

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On the Pathological Anatomy of Chorea Minor.—M. RICHARD (*Deutsch. Arch. f. klin. Med.*, 1902, Band lxxii., Heft 5 and 6, p. 504) reports two cases of chorea minor, with detailed histological descriptions. The first case followed an attack of acute articular rheumatism, while the second case was characterized by previous attacks of chorea. At autopsy an acute endocarditis was found in both cases, due probably in the first case to the staphylococcus pyogenes aureus, and in the second to the streptococcus pyogenes. A bacteriological examination was made of the fluid from the ventricles of the brain in both cases, with practically negative results. The nervous system in neither case presented any gross pathological changes, but microscopically there was a degeneration of both anterior and posterior root fibres in the cord, and even more marked alterations in the brain. No lesions were found in the spinal ganglia. Throughout the brain there was a small-cell infiltration, most marked in the perivascular spaces; this invasion in places extended over moderately large areas. Small hemorrhages were also found, appearing most numerous in the region of the basal ganglia and beneath the ependymal cells of the ventricles. Within the last few years Pianese has described an "ependymyelitis" occurring in a case of chorea minor, and Neuwerck has called attention to areas of inflammation and hemorrhage in a similar case. The author believes the changes which he reports should be considered as dependent upon a general toxæmia.—W. T. L.

Bacteria in the Bile Passages of Dogs.—GILBERT and LIPMAN (*Presse Médicale*, June 18, 1902), at a meeting of the Société de Biologie, report their results of a series of bacteriological examinations of the bile passages in dogs. Cultures were taken from the gall-bladder and various parts of the bile ducts, and, while uniformly sterile for aërobes, showed constantly the presence of various anaërobic bacteria. In view of the fact that the bile passages have been supposed to be sterile, and on account of the significance of bacteria in many diseases of the bile passages, the authors regard their results as of more than passing interest.—F. P. G.

On the Transplantation of a Sarcoma of the Thyroid Gland of a White Rat.—LEO LOEB (*Virchow's Archiv*, 1902, Band clxii., Heft 2, p. 175) reports

on the experimental transplantation of portions of a sarcoma of the thyroid gland of a white rat into the abdominal cavity of other white rats. The original tumor was quite vascular, and was further characterized by areas of softening in which secondary hemorrhages were often found. In the first transplantation the tumor nodule became partially necrotic, and was surrounded by a zone of connective tissue. Cells arising probably from the transplanted tumor were found in the connective-tissue zone, where they showed pyknosis and mitosis. When the growth was again transplanted into other rats it gave rise to tumors closely resembling in their structure the original sarcoma. During their development a myxoid degeneration was noted, together with the formation of cysts. By inoculating fluid from these cysts into the abdominal cavity of rats the author succeeded in producing in some cases single sarcomatous nodules, and in others a general sarcomatosis of the peritoneum. Thus successive transplantations were made intraperitoneally and subcutaneously over a period of fifteen months. In all 150 animals were used.

During the development of these tumors it was found that if they became infected their growth was much more extensive than if bacteria were excluded. For instance, a nodule embedded in the deeper subcutaneous tissues of the rat was soon surrounded by connective tissue and ceased to grow, while another nodule which involved the skin and became infected increased rapidly in size and produced extensive contact metastases. Again, it was found that if an incision was made, and small pieces removed from an encapsulated tumor which had stopped growing, rapid growth again took place, with the formation of small metastatic nodules in the surrounding tissues. No metastases ever developed by means of the bloodvessels or lymph channels. Throughout the experiments the sarcoma retained in general its original morphological and physiological characteristics, but certain modifications were observed from time to time. Occasionally the tumor cells assumed the characters of cells from endothelial origin, although the original growth was a spindle-celled sarcoma. By further transplantation, however, the spindle-cell type was again restored. Giant cells were also occasionally found.—W. T. L.

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